ORIGINAL ARTICLE

Validation of an Environmental Exposure Chamber for Assessment of Allergy to Grass Pollen

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Abstract

Background: An environmental exposure chamber (EEC) is a health facility that enables allergic symptoms to be induced in a controlled manner in persons sensitized to a dispersed allergen. We performed a study at our institution to technically and clinically validate an EEC in patients allergic to grass pollen.
Methods: We developed a new EEC inside a clean room (ISO-8 class) measuring 15.6 m². During the technical validation, the patient's exposure conditions were simulated by ensuring homogeneous distribution of the allergen with a particle disperser and monitoring both particle and pollen grain concentrations. Temperature, pressure, and humidity were also registered.
A total of 31 volunteers were exposed to *Phleum pratense* pollen in the EEC. Of these, 25 were allergic (cases), with symptoms of rhinoconjunctivitis with or without asthma, and 6 were not (controls). One control and 2 cases were exposed twice to check reproducibility, generating a total of 34 challenges. The test was stopped once the positivity criterion was reached or the patient completed 90 minutes in the EEC.
Results: Both the stability of particle concentrations and approximation to the pollen sample concentration were guaranteed.
All challenges with controls were negative. Among the cases, 15% of challenges were negative and 85% were positive. No severe or late reactions were observed. Volunteers exposed twice to the same pollen had the same result in both challenges.
Conclusion: Our EEC proved to be a specific, safe, and reproducible tool for the diagnosis of grass pollen allergy.

Key words: Allergen. Environmental exposure chamber. Pollen. Rhinitis. Asthma. Validation.

Resumen

Antecedentes: Una CEA (cámara de exposición ambiental) es una instalación sanitaria que ofrece la posibilidad de inducir síntomas alérgicos de forma controlada en sujetos sensibilizados tras la dispersión de un alérgeno. En el HURyC (Hospital Universitario Ramón y Cajal) se ha llevado a cabo un estudio para conseguir la validación técnica y clínica de una CEA en pacientes alérgicos al polen de gramíneas.
Métodos: En el HURyC, se ha desarrollado una nueva EEC dentro de una sala blanca (clase ISO-8) de 15,6 m². Durante su validación técnica, se simularon las condiciones de exposición de los pacientes, buscando una distribución homogénea del alérgeno con un dispersor de partículas, y monitorizando tanto la concentración de partículas como de granos de polen. También se registraron los valores de temperatura, presión y humedad.
31 voluntarios fueron expuestos al polen de *Phleum pratense* en la CEA, de los cuales 25 eran alérgicos (casos) con síntomas de rinoconjuntivitis con o sin asma y 6 no eran alérgicos (controles). 1 control y 2 casos fueron expuestos dos veces para comprobar la reproducibilidad, alcanzando un total de 34 provocaciones. Una vez se alcanzaba el criterio de positividad o al cumplir 90 minutos dentro de la CEA, se detenía la prueba.
Resultados: Se garantizaron tanto la estabilidad de la concentración de partículas como su aproximación a la concentración de polen muestreada. Todas las provocaciones a los controles fueron negativas. Entre las provocaciones de los casos, el 15% fueron negativas y el

85% positivas. No se observaron reacciones graves ni tardías. Los voluntarios expuestos dos veces al mismo polen obtuvieron el mismo resultado en ambas provocaciones.
Conclusión: La CEA del HURyC ha demostrado ser una herramienta específica, segura y reproducible en el diagnóstico de la alergia al polen de gramíneas.

Palabras clave: Alérgeno. Cámara de exposición ambiental. Polen. Rinitis. Asma. Validación.

Summary box

- **What do we know about this topic?**
  Environmental exposure chambers (EECs) have been used in randomized clinical trials and play an important role in studies of allergic rhinitis by providing a fixed concentration of allergen in a controlled environment.
- **How does this study impact our current understanding and/or clinical management of this topic?**
  Our EEC provided an effective method for the assessment of allergic rhinitis and asthma due to *Phleum pratense*. It is a perfect tool for triggering allergic symptoms under controlled conditions, being suitable for both clinical diagnosis and research.

Introduction

Allergic rhinitis affects 1 in 5 people worldwide and is associated with consequences such as diminished quality of life and loss of productivity. Although diverse treatment options are available, some patients remain undertreated or affected by drug adverse effects. Rhinoconjunctivitis and asthma in patients who are sensitized to multiple pollens constitute a challenge for diagnosis and treatment, since there exists a need to identify the relationship between the load of a specific allergen and the patient's symptoms. Moreover, pollination may occur at the same time of the year for different species. Therefore, a greater understanding of etiological agents and their pathological mechanisms may help to ensure targeted treatment [1-5].

Environmental exposure chambers (EECs) are generally considered safe, effective, and suitable for conducting randomized clinical trials of new allergy treatments [3].

EECs have become increasingly important in clinical research, particularly for studies of allergic rhinitis [4]. They provide a fixed concentration of allergen in a closed and tightly controlled environment [5].

Even though EECs have been widely used in phase 2-4 clinical trials for more than 3 decades, their technical configurations differ depending on the country, making it difficult to conduct large multicenter allergen immunotherapy studies. Regulatory authorities require harmonization of clinical assessments and documentation when clinical outcomes obtained using EECs are compared with those obtained from environmental exposures [4,6-9].

This study was designed to validate and assess the efficacy and safety of grass pollen challenge at our center in patients with grass pollen–induced allergic rhinitis with and without associated asthma. The aims of the study were to determine the clinical validity of grass pollen administration and its effect on symptom scores, to determine the optimal amount of grass pollen particles to induce significant allergic symptoms equivalent to those induced via natural exposure, and to demonstrate the safety and reproducibility of the results under stable environmental conditions [4-6,10-15].

Challenge tests, such as exposure to allergens in a chamber, are used to assess respiratory symptoms (rhinoconjunctivitis and asthma), confirm a diagnosis, and evaluate the effectiveness of drugs, with a moderate positive predictive value and excellent negative predictive value, if performed by experienced investigators [16]. The number of immunomodulatory therapies for asthma is rising steadily. However, these therapies are only cost-effective in selected patients exhibiting very specific characteristics. Consequently, there is a demand for more clinical instruments to be used in phenotyping [17]. As patients with mild and moderate asthma require daily management, the EEC could be a useful tool for assessment.

EECs improve clinical diagnosis and enable differentiation of immunologically sensitized patients from clinically reactive ones. They have contributed to our understanding of the pathophysiology and diagnosis of allergic rhinoconjunctivitis and allergic asthma, as well as the pharmacological properties, efficacy, duration, and onset of action of new therapeutic options [6,18].

The chambers were developed in the 1980s to test patients with pollen allergy under controlled and reproducible conditions of pollen exposure [5]. At that time, models for grass, ragweed, birch pollen, and house dust mites were established. The way that patients are challenged in the EEC offers an advantage over natural seasonal exposure, because confounding conditions, such as wind and rain, may influence pollen counts [19].

The EEC model was approved by the United States Food and Drug Administration and the European Medicines

Agency (EMA) for phase 2 immunotherapy trials and proposed by the EMA for dose-finding trials in immunotherapy [20-22]. The EMA also stated that in pivotal phase 3 trials with immunotherapy, EECs were a promising tool for evaluating efficacy but that they require further clinical validation [20,22].

As the number of studies with EECs increases, it has become evident that defining the characteristics of each chamber in a standardized way and harmonizing protocols for this type of study will improve the quality of the data acquired. This information can then be applied to determine the safety and efficacy profile of new therapies. A first position paper to pave the way for international harmonization of the EEC and to promote its more widespread use in clinical trials was published in 2017 [23]. In 2021, a position paper of the European Academy of Allergy and Clinical Immunology suggested the need for technical validation of various allergen models, airborne allergen concentrations, diameter of the allergenic particles, pollen grain counts, stability of the exposure, and climatic conditions of the EEC. It also important to identify optimal antistatic, nonadhering, and easy-to-clean materials and well-defined cleaning procedures. Finally, it is necessary to register standardized and clinically relevant outcomes [5].

The EEC developed at Ramón y Cajal University Hospital (RyCUH), Madrid, Spain is based on pre-existing chambers with the same objective, namely, to enable distribution of pollen inside the room in a reproducible, homogenous, and precise manner [5,6,24]. In contrast with current EECs, the main interest of health care professionals at RyCUH is the evaluation of both asthma-related symptoms and nasal symptoms for diagnostic purposes.

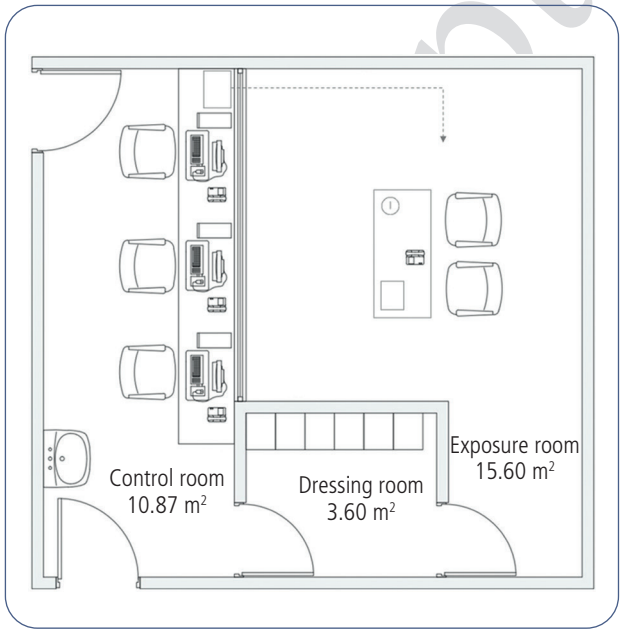

Figure 1. Distribution of the environmental exposure chamber. This chamber was classified and certified as a Class 8 room according to the ISO 14644-1 standard.

2. Material and Methods

2.1. Environmental Exposure Chamber

A new EEC was developed within the Allergy Unit of RyCUH. As shown in Figure 1, this facility consists of the following: a main room measuring 15.60 m^2, in which the allergen exposures take place; a control room, from which the complete process be monitored; and a dressing room which is used for both entry and exit. Negative pressure inside the chamber prevents contamination of areas outside the chamber.

The exposure chamber has its own ventilation system, consisting of 3 grilles placed in the ceiling (with Camfil F7 and Ecopleat G filters) (1 for impulsion and 2 for extraction). These enable an air flow to ensure homogeneous distribution of pollen throughout the room. The filters prevent air contamination inside and outside the chamber. The system allows 5 different configurations (Supplementary Table S1).

Particle dynamics were studied to configure the arrangement of patients and objects in the room so that the scenarios were reproducible (Supplementary Fig. S1 and S2).

A solid SAG 410 aerosol generator (Topas GmbH) was used to disperse the pollen. This was connected to the EEC via a plastic dispersion tube. Pollen was transported through this tube via air propelled by a compressor, also located in the control room. The pollen used (*Phleum pratense*, ALK-Abelló S.A.) was stored at –18°C until use.

An airborne particle counter (SOLAIR© Boulder Counter) was used to monitor the particle concentration (particles/m^3) inside the exposure room within a specific range of diameters. In this case, particles measuring 25-40 µm were used, since this was the closest approximation to the diameter of *P pratense* particles. A personal volumetric air sampler (Burkard Manufacturing Co. Ltd) was used to take air samples for periods of 15 minutes to make an approximation of the real pollen grain concentration. Therefore, these samples were collected on glass slides impacted by the pollen grains for evaluation using an optical microscope (Supplementary Fig. S3).

2.2. EEC Staff, Safety, and Noncontamination Measures

The facility has at least 3 dedicated staff: a technician, who supervises and controls the devices and monitors the experiment, and health care staff (a nurse and a doctor from the allergy department), who monitor the patients' condition during the study.

Before entering the room, patients put on protective clothes (overalls, shoe covers, cap) in order to prevent exterior contamination and carriage of allergens out of the chamber after exposure [5,24].

During trials, the patients remain in continuous communication with health care staff. In addition, they fill out a series of symptom scoring tests, which are visible in real time to the attending personnel. The team is fully trained to monitor the patients' vital signs, respiratory function, feedback, and adverse events throughout the procedure. In the case of an emergency, patients can be moved immediately to the observation room (next to the EEC), where all the necessary equipment is available.

Cleaning protocols have been established and are included in the supplementary information.

2.3. Methods for Technical Assessment

The proper functioning of the EEC was analyzed with a dual objective: to ensure safety and to verify the reproducibility of environmental conditions inside. Therefore, 15 trials were performed to ensure the stability of the various environmental parameters (temperature, relative humidity, and differential pressure, which was maintained negative to prevent the release of contaminants from the EEC) and the concentration of particles and pollen grains in the air.

These tests lasted 90 minutes, during which time the estimated amount of pollen was introduced into the room through the solid aerosol generator. Before pollen was expelled, the particle concentration in the room was measured to ensure the absence of air contamination.

The amount of pollen released in the room was manually regulated on demand, based on the particle concentrations provided periodically by the particle counter. Additionally, the volumetric air sampler was used to collect air samples at 15-minute intervals, allowing for the subsequent calculation of the actual pollen concentration. Temperature, relative humidity, and differential pressure parameters were also monitored during the 90-minute simulation.

We focused on provoking symptoms while ensuring patient safety with a shorter exposure time than reported elsewhere, since the purpose of this tool was to be used in routine clinical practice [25].

2.4. Clinical Validation Study

2.4.1. Participants

The cases comprised patients with rhinoconjunctivitis with and without asthma recruited from the Allergology Department of the RyCUH between December 2022 and February 2024. The inclusion criteria were as follows:

- Positive skin prick test results against grass pollen (*P pratense*), defined as a wheal diameter equal to or greater than that of the histamine control and a negative saline control.
- Being asymptomatic in the previous month without allergy treatment.
- Not having received immunotherapy in the previous 5 years, regardless of the composition of the extract
- Signed informed consent.

The study was performed out-of-season, with no priming period or screening exposures to remove low responders. Exposure to grass pollen in the chamber was in autumn, that is, several months after the grass pollination season in Madrid (April-June) [26].

The controls comprised patients allergic to allergens other than grass pollen and healthy nonallergic patients.

In addition, 7 cases were exposed to placebo inside the chamber before the challenge.

The study was approved by the Bioethics Committee of RyCUH, with record number 445, dated 20-12-2022.

2.4.1.1. Clinical Endpoints

Our objective was to prove that the RyCUH chamber could induce respiratory symptoms in at least 60% of patients with grass pollen allergy, according to previous studies [27].

The interest of the chamber lies in observing the clinical reaction in patients sensitized to grass pollen.The study used the following records and questionnaires: Total Nasal Symptom Score (TNSS), Total Ocular Symptom Score (TOSS) [28], a specific asthma survey, and a visual analog scale (VAS) to assess nasal and general symptoms.

We used the TNSS published initially by Krug et al [25] and later modified by Downie et al [29] for EECs.

Meters were used to assess peak nasal inspiratory flow (PNIF) (In-check, Clement Clarke International Ltd) and peak expiratory flow (PEF) (Mini Wright, Clement Clarke International Ltd) [30].

2.4.2. Monitoring Procedure

To be eligible for allergen exposure, all patients had to be asymptomatic within the previous month and with normal nasal and pulmonary function ($FEV_1 \geq 75\%$) at the time of the study. They had to have been off antihistamines during the week prior to the exposure and off intranasal or inhaled corticosteroids for 14 days before the exposure [4,14]. Pregnant women were excluded. Clinical assessment and questionnaire training were undertaken before the challenge, and FEV_1 was measured before and after the challenge, as was fractional exhaled nitric oxide (FeNO) (NIOX VERO, Circassia AB).

Every 15 minutes or as required, patients reported their symptoms through the previously mentioned questionnaires (VAS, TOSS, TNSS), bronchial function was assessed using an asthma-specific survey and PEF, and nasal function was monitored through PNIF. Patients with a positive exposure were treated until complete disappearance of symptoms and kept under observation for up to 2 hours. Patients with a negative exposure were kept under direct surveillance for 2 hours. Patients were discharged once they were confirmed as being asymptomatic for at least 2 hours after exposure. At home, they were monitored with PEF every 2 hours until the following morning, except during sleep, and were trained to administer treatment if symptoms recurred. The purpose of the follow-up was to assess the safety of the test, once concluded.

Patients were exposed for a maximum of 90 minutes or until they reached the positivity criteria for rhinitis or asthma or TOSS ≥5. The positivity criteria for rhinitis were as follows: a TNSS ≥6 or nasal VAS ≥5 or decrease in PNIF ≥40%. For conjunctivitis, the criterion was a TOSS ≥3. For asthma, the positivity criteria were either a decrease in peak expiratory flow rate ≥15% or a decrease in FEV_1 ≥20% and bronchial symptoms.

As described by Khayath et al [27], an early asthmatic reaction was defined as a 20% decrease in FEV_1 compared to the pre-exposure FEV_1. A late asthmatic reaction was defined as a 15% decrease in FEV_1 or a 20% decrease in peak flow detected 1-6 hours after the early asthmatic reaction.

2.4.3. Statistical Analysis

Descriptive statistics for continuous variables are presented as mean (SD) when the distribution is normal or as median (IQR) when it is not. Normality was determined using the Kolmogorov-Smirnov test. Categorical variables are presented as frequencies or percentages.

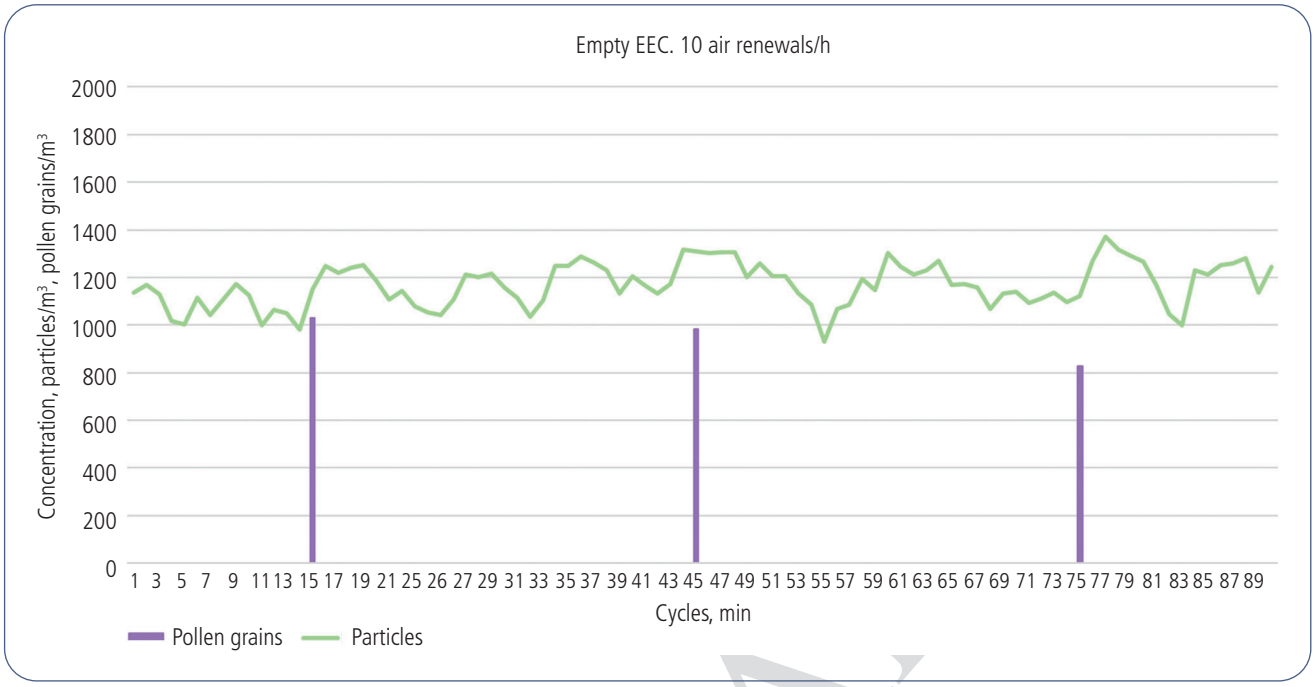

Figure 2. Average concentrations of particles and pollen grains measured over 17 simulations.

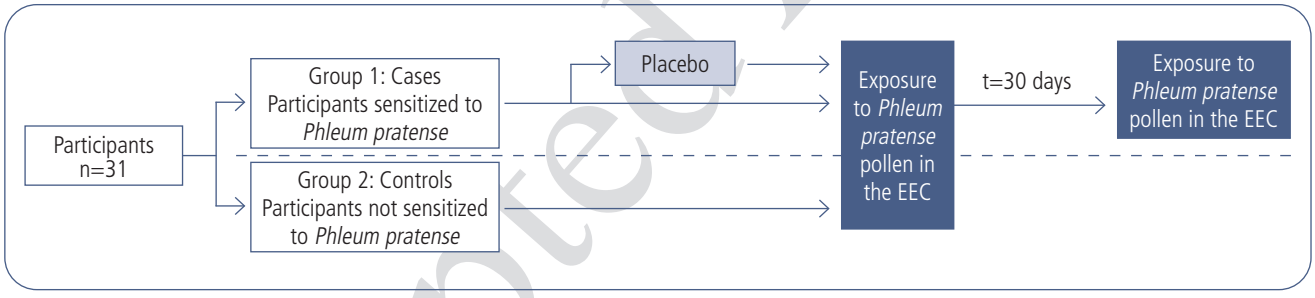

Figure 3. Study design.

Continuous variables were compared using an unpaired t test for parametric variables or the Mann-Whitney test for nonparametric variables. The χ^2 test or Fisher exact test was used for categorical variables.

A P value <.05 was considered significant. All P values reported are 2-sided. The analyses were performed using IBM SPSS Statistics 20.0 (IBM Corp.).

3. Results

3.1. Technical Parameters

After 17 pollen dispersion sessions in the empty EEC, both the stability of the particle concentration (1170 [90] particles/m³) and the sampled pollen concentration (940 [100] grains/m³) were guaranteed (Figure 2). The results for temperature, relative humidity, and differential pressure measurements are shown in Supplementary Figure S4.

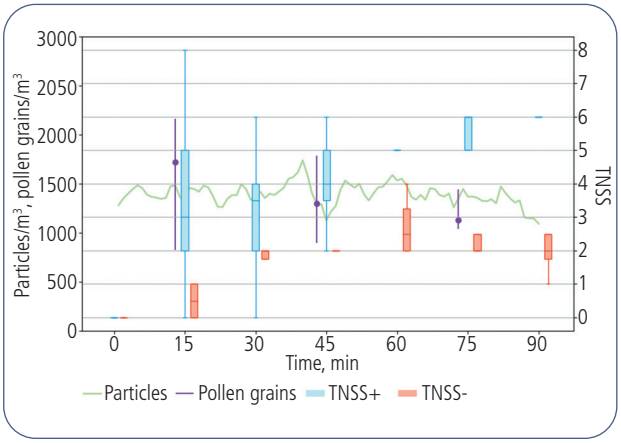

Figure 4. Average particle and pollen concentrations and TNSS results (both positive and negative) during exposure to *Phleum pratense*. TNSS indicates Total Nasal Symptom Score.

3.2. Clinical Study

A total of 31 volunteers were recruited. Of these, 6 were controls (3 nonallergic individuals, 1 individual sensitized to Cupressaceae and *Olea europaea*, 1 individual sensitized only to *O europaea*, and 1 individual sensitized to house dust mites) (Figure 3). The remaining 25 cases were diagnosed with allergic rhinitis (8 with asthma and sensitized to grass pollen). Three participants (1 control and 2 cases) were exposed twice to the same concentration of grass pollen with a wash-out period of at least 4 weeks. The mean age was 31.04 (10.55) years. The mean wheal diameter for the *P pratense* response (skin prick test) was 8.12 mm (3.35 mm), and the median specific IgE was 20.25 kU/L (4.87-42.38 kU/L). Across the exposure sessions, the median pollen level was 1541.5 (850.8-1910.8) grains/m^3, and the mean concentration of particles was 1415 (339) particles/m^3 (Figure 4).

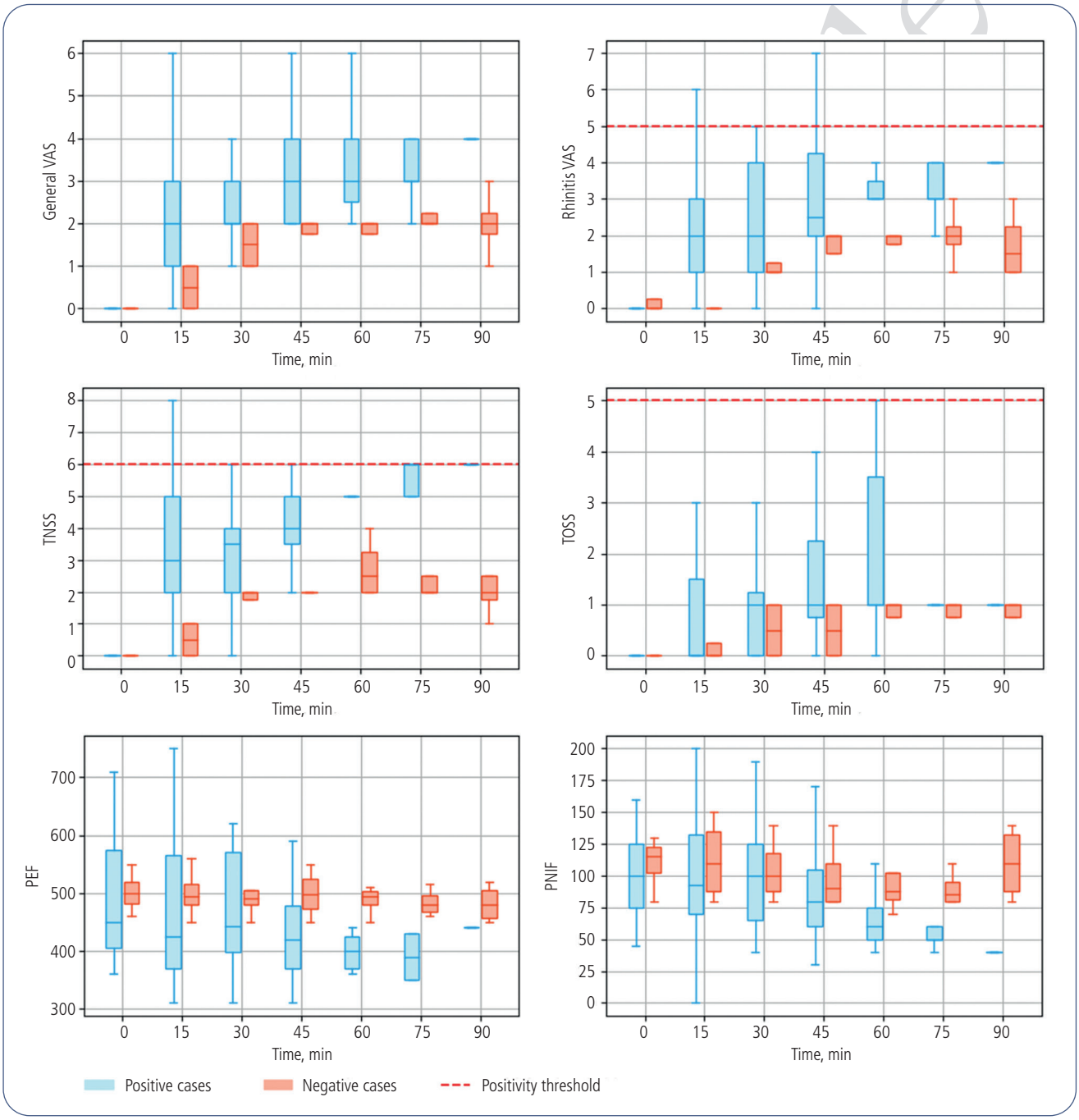

Figure 5. Results of the symptom tests for both positive and negative cases during exposure to *Phleum pratense* in the environmental exposure chamber. VAS indicates visual analog scale; TNSS, Total Nasal Symptom Score; TOSS, Total Ocular Symptom Score; PEF, peak expiratory flow; PNIF, peak nasal inspiratory flow.

3.3. Clinical Endpoints

All 31 volunteers were exposed (6 controls [nonallergic to grass pollen], 25 cases [allergic to grass pollen]). One control and 2 cases were exposed twice to the pollen to guarantee reproducibility, reaching a total of 34 challenges (7 for controls, 27 for cases). None of the 7 challenges for controls elicited symptoms, while among the 27 challenges for cases, 4 were classified as negative (15%) and 23 (85%) were classified as positive. In all 23 positive challenges (100%), the participant had rhinitis. Sixteen (69%) also presented conjunctivitis, and only 4 (17%) presented an early asthmatic reaction. All the patients presented an early allergic reaction, and all the reactions were treated and resolved in the following hour. No late allergic reactions or ocular-nasal or asthma symptoms were detected during the 24 hours after the challenge. Volunteers classified as negative remained in the EEC for a period of 90 minutes, while those classed as positive remained for a mean of 48.9 (28.3) minutes.

Figure 4 shows the average levels for particles measuring between 25 μm and 40 μm, as well as the mean pollen grain values and TNSS during exposures (see Supplementary Table S2).

In the positive challenges, the median TNSS was 6 (6-7); in the negative challenges, the median TNSS was 1.5 (0.25-2). The remaining results are shown in Supplementary Table S2.

The results (both positive and negative) of all tests (VAS, TNSS, TOSS, PEF, and PNIF) during the exposure period are shown in Figure 5.

3.4. Specificity

No control volunteers developed symptoms during their test. Moreover, 7 cases were exposed to placebo inside the chamber without developing symptoms.

4. Discussion

The objective of this study was to describe and evaluate a new system for controlled exposure to allergens in an EEC in a hospital environment. The results demonstrated that the system was able to deliver an average pollen level, as reported elsewhere [24], making it possible to reproduce typical symptoms of seasonal allergic rhinitis out of season. The target exposure level is low compared with other EEC studies [31], although it is similar to and based on the EEC described by Kenney et al [24].

Importantly, the use of protective clothing in this study may promote a feeling of being in a clinical setting rather than in a situation where participants are free to wear their own clothes. However, for this study we used protective clothing to ensure that once participants had left the EEC, they were no longer exposed to pollen, because that could have affected the outcome of the study.

Our in-hospital EEC was able to generate reproducible pollen concentrations comparable to those seen in other facilities. Validation studies systematically identified appropriate dispersion levels that elicit sufficient symptoms [26]. In the RyCUH EEC, with a median pollen level of 1541.5 grains/m^3, symptoms were reported without severe adverse effects in most allergy patients, as well as in both the allergic and nonallergic volunteer groups. Consistent with other authors, we used various pollen concentrations (eg, 1000, 2000, 4000, and 8000 grass pollen grains/m^3) and observed a significant effect of pollen concentration on symptom severity [25].

A positive finding was that in the present study, around 1500 grains/m^3 induced allergic symptoms, which is a lower concentration than that described by Krug et al [25].

As in previous studies [12,13], the subjective results obtained with TNSS and TOSS and the results of the survey administered during the challenges, as well as objective parameters (eg, spirometry, PEF, and PNIF), were measured as secondary outcomes. The results were highly reproducible in all the patients tested.

PEF and FEV_1 were measured during the challenge to assess safety. In addition, all the participants measured PEF at home during the following 24 hours and were contacted 24 hours after the test, as reported elsewhere [12,13].

Given that the positivity criteria described in the literature are very heterogeneous, we analyzed different values and questionnaires, concluding that the TNSS is the value that best approximates the positivity of the challenge and enables the patient to leave the chamber with moderate symptoms, thus avoiding onset of severe symptoms.

All the patients with positive challenge results in our study were able to control their symptoms with medication in the hour following the end of the test, with no fatal reactions. Moreover, none of them experienced late reactions, and they could all be discharged home without incidents or reactions within 24 hours. Authors of similar studies based on EEC challenge with allergens such as birch or cat pollen reported 16%-32% of late allergic reactions [4,15]. This difference could be explained by our shorter challenge time, since our objective was to identify allergic symptoms

In summary, the results obtained support the feasibility of stable environmental conditions within the EEC, thus rendering it a viable choice for inclusion in clinical studies.

The number of immunomodulatory treatments for asthma is rising steadily. However, these are only cost-effective in selected patients with very specific characteristics. Consequently, there is a demand to raise the number of clinical instruments available for phenotyping [17]. Patients with mild and moderate asthma require daily management, in which EECs could prove useful.

5. Conclusions

Under maintained temperature, humidity, and pressure during challenges, the concentration of pollen remained stable at the targeted values. The RyCUH EEC enabled precise, safe, specific, and homogeneous distribution of pollen, constituting an effective method for the assessment of allergic rhinitis and asthma due to *P pratense*. We demonstrated that the EEC is a perfect tool for triggering allergic symptoms under controlled conditions, indicating that it could be used in both clinical diagnosis and future research in the field.

Acknowledgments

This paper was read and approved by all authors.

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– Kinetics of biomarkers and metabolomics in patients with respiratory allergy due to grass pollen in an environmental exposure chamber.
– Technical and clinical validation of an innovative environmental exposure chamber.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Previous Presentations

An abstract of this case report was submitted to the 2023 Spanish Society of Allergology and Clinical Immunology (SEAIC) Congress and to the 2024 European Academy of Allergy and Clinical Immunology (EAACI) Congress. The case won a poster prize at the EAACI 2023 Hybrid Congress.

References

1. Silver JD, Spriggs K, Haberle S, Katelaris CH, Newbigin EJ, Lampugnani ER. Crowd-sourced allergic rhinitis symptom data: The influence of environmental and demographic factors. Sci Total Environ. 2020;705:135147.
2. Horak F, Jager S. The Vienna challenge chamber (VCC)—a new method for allergen exposition tests. Wien Klin Wocheschr. 1987;99:509-10.
3. Devillier P, Le Gall M, Horak F. The allergen challenge chamber: a valuable tool for optimizing the clinical development of pollen immunotherapy: The allergen challenge chamber and pollen immunotherapy. Allergy. 2011;66(2):163-9.
4. Gherasim A, Dietsch F, Beck M, Domis N, de Blay F. Birch-induced allergic rhinitis: Results of exposure during nasal allergen challenge, environmental chamber, and pollen season. World Allergy Organ J. 2023;16(7):100801.
5. Pfaar O, Bergmann K-C, Bonini S, Compalati E, Domis N, de Blay F, et al. Technical standards in allergen exposure chambers worldwide - an EAACI Task Force Report. Allergy. 2021;76(12):3589-612.
6. Zieglmayer PU, Pfaar O. Update on the use of allergen challenge chambers in immunotherapy: clinical implications. Curr Opin Allergy Clin Immunol. 2022;22(2):132–6.
7. Valero A, Justicia JL, Antón E, Dordal T, Fernández-Parra B, Lluch M, et al. Epidemiology of allergic rhinitis caused by grass pollen or house-dust mites in Spain. Am J Rhinol Allergy. 2011;25(4):e123-8.
8. Arnedo-Pena A, Romeu-Gracia MA, Bellido-Blasco JB, Meseguer-Ferrer N, Silvestre-Silvestre E, Conde F, et al. Incidence of allergic rhinitis in a cohort of young adults from 13-15 years old to 23-25 years old in Castellon (Spain). Allergol Immunopathol (Madr). 2017;45(3):2517.
9. González-de Paz L, Valdesoiro-Navarrete L, Roma J, Blat-Guimerà E, Benavent-Areu J, Bartra J, et al. Prevalence and Impact of Asthma and Allergy on Daily Life, Health Outcomes and Use of Healthcare Services in Children: A Population-Based Study. Arch Bronconeumol. 2023;59(8):4817.
10. de Blay F, Gherasim A, Casale TB, Doyen V, Bernstein D. Which patients with asthma are most likely to benefit from allergen immunotherapy? J Allergy Clin Immunol. 2022;149(3):833-43.
11. Koriyama M, Okamoto Y, Suzuki T, Iinuma T, Yamamoto H, Okuma Y, et al. Characteristics of Japanese cypress pollen-induced allergic rhinitis by environmental challenge chamber. Allergol Int. 2022;71(1):144-6.
12. Kosowska A, Zemelka-Wiącek M, Smolińska S, Wyrodek E, Adamczak B, Jutel M. Clinical validation of grass pollen exposure chamber in patients with allergic rhinitis triggered by timothy grass. Clin Exp Allergy. 2024;54(7):489-99.
13. Zemelka-Wiacek M, Kosowska A, Winiarska E, Sobanska E, Jutel M. Validated allergen exposure chamber is plausible tool for the assessment of house dust mite-triggered allergic rhinitis. Allergy. 2023;78(1):168-77.
14. Zemelka-Wiacek M, Kosowska A, Jutel M. Symptom Assessment of Patients with Allergic Rhinitis Using an Allergen Exposure Chamber. J Vis Exp. 2023;(193).
15. Piotin A, Godet J, Domis N, de Blay F. Rhinoconjunctivitis severity induced by cat exposure influences early and late asthmatic responses: Evidence from an environmental exposure chamber. Clin Exp Allergy. 2024;54(8):596-606.
16. de Blay F. Provocation tests as measure of efficacy and dosage. Allergy. 2011;66 Suppl 9:47-9.
17. Agache I, Antolin-Amerigo D, de Blay F, Boccabella C, Caruso C, Chanez P, et al. EAACI position paper on the clinical use of the bronchial allergen challenge: Unmet needs and research priorities. Allergy. 2022;77(6):1667-84.
18. North ML, Soliman M, Walker T, Steacy LM, Ellis AK. Controlled Allergen Challenge Facilities and Their Unique Contributions to Allergic Rhinitis Research. Curr Allergy Asthma Rep. 2015;15(4):11.
19. Montoro J, Antolín-Amérigo D, Artés M, Izquierdo-Domínguez A, Zapata JJ, Mur P, et al. Impact of climate change-related environmental factors on the allergens production and the epidemiology and severity of allergic pathologies. J Investig Allergol Clin Immunol. 2024 Jan 11;0.
20. Pfaar O, Agache I, de Blay F, Bonini S, Chaker AM, Durham SR, et al. Perspectives in allergen immunotherapy: 2019 and beyond. Allergy. 2019 Dec;74 Suppl 108:3-25.
21. Overview of comments received on draft guideline on the development of products for specifc immunotheray for the treatment of allergic disease. https://www.ema.europa.eu/en/documents/other/overview-comments-received-draft-guideline-development-products-specifc-immunotheray-treatment-allergic-disease_en.pdf.
22. Rösner-Friese K, Kaul S, Vieths S, Pfaar O. Environmental exposure chambers in allergen immunotherapy trials: Current status and clinical validation needs. J Allergy Clin Immunol. 2015;135(3):636-43.
23. Pfaar O, Calderon MA, Andrews CP, Angjeli E, Bergmann KC, Bønløkke JH, et al. Allergen exposure chambers: harmonizing current concepts and projecting the needs for the future - an EAACI Position Paper. Allergy. 2017;72(7):1035-42.

24. Kenney P, Bønløkke J, Hilberg O, Ravn P, Schlünssen V, Sigsgaard T. Method for a homogeneous distribution of pollens in an environmental exposure chamber. Clin Exp Allergy. 2016;46(9):1176-84.
25. Krug N, Hohlfeld JM, Larbig M, Buckendahl A, Badorrek P, Geldmacher H, et al. Validation of an environmental exposure unit for controlled human inhalation studies with grass pollen in patients with seasonal allergic rhinitis. Clin Exp Allergy. 2003;33(12):1667-74.
26. Jacobs RL, Harper N, He W, Andrews CP, Rather CG, Ramirez DA, et al. Responses to ragweed pollen in a pollen challenge chamber versus seasonal exposure identify allergic rhinoconjunctivitis endotypes. J Allergy Clin Immunol. 2012;130(1):122-7.e8.
27. Khayath N, Doyen V, Gherasim A, Radu C, Choual I, Beck N, et al. Validation of Strasbourg environmental exposure chamber (EEC) ALYATEC(®) in mite allergic subjects with asthma. J Asthma. 2020;57(2):140-8.
28. Schoenwetter W, Lim J. Comparison of intranasal triamcinolone acetonide with oral loratadine for the treatment of patients with seasonal allergic rhinitis. Clin Ther. 1995;17(3):479-92.
29. Downie SR, Andersson M, Rimmer J, Leuppi JD, Xuan W, Akerlund A, et al. Symptoms of persistent allergic rhinitis during a full calendar year in house dust mite-sensitive subjects. Allergy. 2004;59(4):406-14.
30. Augé J, Vent J, Agache I, Airaksinen L, Campo Mozo P, Chaker A, et al. EAACI Position paper on the standardization of nasal allergen challenges. Allergy. 2018;73(8):1597-608.
31. Ellis AK, Soliman M, Steacy LM, Adams DE, Hobsbawn B, Walker TJB. Clinical validation of controlled exposure to birch pollen in the Environmental Exposure Unit (EEU). Allergy Asthma Clin Immunol. 2016;12:53.

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