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Responsiveness to timothy grass pollen in individuals without known natural exposure in an allergen challenge chamber

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ABSTRACT

Background: The responsiveness to a nonendemic grass species is unknown and cannot be research without an allergen challenge chamber.

Objective: To determine the clinical responsiveness to timothy grass pollen (TGP) in participants without known natural exposure in an allergen challenge chamber (ACC).

Methods: Of the 26 screened participants, 22 met screening criteria and completed the 2 chamber exposures. The study consisted of an initial screening visit that included a blood draw for serum specific IgE (ssIGE) to Bermuda grass pollen and TGP followed by a 4½-day run-in phase and two 3-hour ACC exposure visits. This study was performed early in the first week of December 2013, when no seasonal pollens were detected in San Antonio, Texas. Symptom scores were recorded at baseline and every 30 minutes.

Results: Of the 26 screened participants, 22 met the screening criteria and completed the 2 chamber exposures. Thirteen participants had always lived in South Texas without natural exposure, and 9 had previously lived in areas with TGP exposure. All participants tested positive to TGP and Bermuda grass pollen. Twelve and 13 of 22 had positive ssIgE test results to Timothy and Bermuda allergens, respectively, with 11 having positive results for both allergens. There were strong correlations among skin prick test size, a positive ssIgE test result, and high symptoms from TGP exposure. There was little difference in symptoms between those who had lived their entire lives in South Texas and those who had lived elsewhere.

Conclusion: In Texas, where exposure to TGP is minimal, strongly positive SPT and ssIgE test results were predictors of high symptoms to TGP exposure. Never exposed participants in South Texas reacted to TGP similar to those who had previous natural exposure, suggesting that in vivo cross-reactivity may be higher than predicted by prior in vitro data and may allow the use in clinical trials of allergens not endemic to the locale of an ACC.

Introduction

Allergen challenge chambers (ACCs) have been previously used to determine the efficacy and onset of action of new therapies for allergic rhinitis study and asthma.[1,7,9–11] These facilities offer many advantages over traditional research methods in that studies can be performed outside the natural pollen seasons, allergen levels can be carefully controlled and monitored in the chamber with no effect from outside weather conditions, and study participants are carefully monitored while being exposed to allergen.

Grass pollen sensitivity is a major cause of allergic rhinoconjunctivitis throughout the world, affecting most atopic individuals.[2] Asthma, atopic dermatitis, and, rarely, contact dermatitis may also occur as a result of exposure to these pollens. Management of these symptoms may be only partially effective, with treatments ranging from symptomatic (attempting to control symptoms) to specific (attempting to alter the individuals level of sensitivity).[3]

Exposure to the pollinating grass species is not evenly distributed and varies according to the climate of the geographic areas.[2] Temperate grasses dominate the northern parts of North America and Europe, with subtropical grasses dominating the warmer climates of parts of Africa, India, Asia, Australia, and Central and South America and the Southern United States.[1] Even though in vitro studies have found significant cross-reactivity among various grass species, no in vivo clinical trials using nonendemic grasses have been performed.

In this investigation, we sought to determine the extent to which allergic symptoms induced by a challenge to timothy grass

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Table 1
Subject inclusion and exclusion criteria

Inclusion Criteria
Male or female 18 to 70 years of age
History of AR to grass pollen exposure and a SPT result to Bermuda grass of ≥5 mm greater than the diluents control
Exclusion criteria
Female who is pregnant or lactating
Have any significant medical illness that may interfere with the study
Have any abnormalities on physical examination that may interfere with the study
Had a respiratory infection during the past 14 days before the screening visit
Current medical history of pulmonary disease requiring daily drug therapy or asthma requiring treatment >2 times per week
Has participated in a trial with an investigational drug in the last 30 days
History of rebound nasal congestion from extended use of topical decongestants
History of nasal polyps, septal perforation, or significant nasal tract malformations noted on physical examination
Current alcohol or drug abuse or history of the same in the past 3 years
Use of disallowed medications
Immunotherapy within 90 days of screening visit

Abbreviations: AR, allergic rhinoconjunctivitis; SPT, skin prick test.

pollen (TGP), a temperate grass, in an ACC located in South Texas would mimic the symptoms that would be naturally induced by pollens of subtropical grasses (Bermuda, Bahia, or Johnson grass pollens). The choice of TGP was based on its wide prevalence, the intense symptoms elicited in its endemic regions, and the increasing use of its pollen in new approaches to therapy.

Currently, there is great interest in novel allergy therapies, including safer modes of immunotherapy, such as sublingual immunotherapy. Two new grass sublingual immunotherapy products, Oralair (a tablet containing extracts from sweet vernal, orchard, perennial rye, timothy, and Kentucky blue grass)[4] and Grastek (a tablet containing timothy grass extract)[5] have recently been approved for use in the United States by the Food and Drug Administration for the treatment of grass allergy to one of the component grasses in the product. The grass species included in these grass tablets belong to the subfamily Pooidea, which are the dominant grasses in the temperate zones of the world but account for less than 15% to 25% of the grasses in the subtropical Southern United States.[6] By contrast, the most prevalent grasses in central Texas belong to the subfamilies Chorioideae (Bermuda grass) and Panicoideae (Johnson grass and Bahia grass).[6]

As in our previous investigation with ragweed,[7] the successful use of a nonendemic allergen was an important objective because sufficient cross-reactivity could allow for testing the efficacy of novel therapies against an allergen in an ACC in which the species of pollen being tested is different from the species that would be used for treatment.

Methods

Study Participants

The protocol, amendments, and informed consent documents were approved by the IntegReview Institutional Review Board (Austin, Texas). All participants provided written informed consent, and the study was conducted according to Good Clinical Practice standards. Twenty-six participants were screened, and 22 participants met all the study inclusion and exclusion criteria (Table 1) and completed the study. Of the 26 screened participants, 22 met screening criteria and completed the 2 chamber exposures.

Study Design

The study design consisted of an initial screening visit followed by a 4½-day run-in phase and two 3-hour ACC exposure visits on 2 consecutive evenings starting at 6 PM. This study was performed early in the first week of December 2013, when no seasonal pollens were detected in San Antonio, Texas. At the screening visit, participants gave informed consent and underwent assessments and procedures that consisted of a medical history review, physical examination, skin prick testing (SPT) to a screening allergen panel, and a blood draw for serum specific IgE (ssIgE) to Bermuda grass pollen and TGP (Phadia ImmunoCAP: negative <0.35 kUA/L) to determine eligibility to participate in the study. A participant run-in diary was distributed to all participants for assessing and recording nasal symptoms, including congestion, itching, sneezing, and runny nose, and ocular symptoms, including itching, tearing, and redness, every morning and every evening using a 5-point Likert scale (scores, 0–4) (Table 2) up to the first chamber exposure. This scale differs from the current 4-point (scores, 0–3) scoring system,[7] which may be too restricted at the 3 (severe) category. Therefore, we elected to use a variation of a 5-point (scores, 0–4) scoring system as suggested by Calderon et al,[8] who also noted that a 0–3-point scale may be inadequate for allergy studies.

Chamber Exposures

Twenty-two participants qualified for inclusion in the study. On confirmation of eligibility and before entry into the ACC, urine pregnancy test results were obtained for all female participants of child-bearing potential. Each participant was assigned a chair and table number for the duration of the consecutive 2-day chamber

Table 2
Likert scale symptom scores

Score	Symptoms	Description
0	Absent	No sign or symptoms evident
1	Mild	Signs or symptoms clearly present but minimal awareness; easily tolerated
2	Moderate	Awareness of signs or symptoms; bothersome but tolerable
3	Severe	Definite awareness of sign or symptoms; hard to tolerate but does not interfere with the activities of daily living
4	Very severe	Difficult to tolerate and interferes with the activities of daily living

Table 3
Participant demographics

Demographic	No. (%) of participants[a]
Age, mean (range), y	42.9 (21–69)
Non-Hispanic white	11
Non-Hispanic black	1
Asian	1
Hispanic white	9
Male sex	12 (54.5)
Lived outside Texas for >5 years	9 (40.9)

[a]Data are presented as number (percentage) of patients unless otherwise indicated.