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Redness response phenotypes of allergic conjunctivitis in an allergen challenge chamber

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ABSTRACT

Background: There are few direct data concerning symptom dynamics of allergic conjunctivitis (AC) in an allergen challenge chamber (ACC).
Objective: To determine the AC dynamics on subsequent exposures to ragweed pollen (RW) in individuals with allergic rhinitis in an ACC. To determine whether consecutive exposures in an ACC have any persistent detrimental ocular physical effects.
Methods: Participants underwent 3 exposures to RW in an ACC. Ocular symptoms of itching and tearing were self-assessed. Ocular redness and lid swelling were assessed by trained ophthalmic technicians. Complete ophthalmic examinations (COEs) were performed by an ophthalmologist.
Results: A total of 188 of 201 participants (93%) developed an ocular redness score of 2 or more in each eye in ACC exposure 1. Reproducibility of redness occurred in approximately 70% of individuals completing ACC exposures 1 through 3. There were no significant changes between baseline COE and end of study COE. Phenotypes were identified by redness responses during and after exposure. Baseline total ocular symptom scores, at 24 hours after a priming exposure, were identified as late-phase reactions rather than enhanced sensitivity.
Conclusion: When assessed by trained professionals, AC was present with a very high frequency in selected individuals allergic to RW monitored in an ACC. Intrasubject reproducibility of redness was consistent across 3 ACC allergen exposures. Phenotypes were identified as early-phase responses, protracted early-phase responses, dual responses, and late-phase responses.
Trial Registration: clinicaltrials.gov Identifier: NCT02079649.

Introduction

Allergic rhinoconjunctivitis (ARC) is a common disorder, affecting up to 40% of the general population in the some westernized countries.[1] Signs and symptoms of the ocular component of ARC, including early-phase responses (EPRs) of itching, tearing, redness, lid swelling, and chemosis, that transition into late-phase responses (LPRs) may cause significant morbidity. However, most natural seasonal studies of ARC have focused on the rhinitis component with less emphasis on ocular itching, tearing, and redness and with almost no consideration of lid swelling, chemosis, and hypererythema, which can be the most disturbing of ocular symptoms. There are few data concerning the frequency and severity of ocular signs and symptoms occurring within the controlled environment of an allergen challenge chamber (ACC) in which relatively high levels of an allergen are sustained for several hours. Likewise, there are neither data concerning LPRs nor any data regarding adverse physical effects extending for a period beyond these sustained exposures. Ellis et al[2] used a quality of life (QOL) survey to evaluate the aftereffects of a 14-hour allergen exposure. Although QOL decreased after the prolonged exposure, it had returned to or improved over baseline within 2.5 weeks. No data were gathered concerning physical effects after exposure.

As very specific forms of allergy intervention evolve, use of an ACC will be necessary to define the various clinical characteristics of these approaches. To our knowledge, there are no published data regarding the dynamics of ocular signs or symptoms elicited in an ACC or the lasting physical effects of such exposures. Careful selection of participants for interventional studies is critical to avoid either enrollment of those with heterogeneous phenotypes of

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responsiveness or unequal distribution of these phenotypes within treatment arms. We endeavored to further understand the dynamics of ocular symptoms elicited during chamber exposures by specifically identifying the response phenotypes and any lingering physical effects after intense, repeated, prolonged exposures. As suggested by the workshop at the National Institute of Health in 2010,[3] we have evaluated the ocular manifestations, with particular focus on redness.

Methods

Selection of Study Participants

The study population included 224 individuals who consented at a single site. Screened participants, selected primarily from allergy databases, were 18 years or older with a history of ARC during the ragweed (RW) season and a skin prick test (SPT) wheal to short ragweed allergen 5 mm or larger compared with the saline control. Participants had a total nasal symptom score of 7 of 12 or greater on a Likert scale during prior natural seasonal studies. There were no natural season ocular severity criteria for participant selection. All participants were ACC allergen exposure naive for recording ocular symptoms. The complete inclusion and exclusion criteria are presented in eTable 1. The protocol, amendments, and informed consent documents were approved by Sterling Institutional Review Board (Atlanta, GA). This clinical study was conducted in accordance with Good Clinical Practice guidelines and applicable regulations.

Ocular Symptom Scoring

Ocular signs and symptoms of redness and lid swelling were assessed by trained ophthalmic technicians (eMethods). Redness was measured using a validated bulbar redness scale[4] (Fig 1). Chemosis was evaluated and scored by ophthalmologists, and itching and tearing were assessed by the study participants (eMethods).

Study Design

An overview of the study design is shown in Figure 2. This study was performed during from July to August when no pollen from any source was detected in San Antonio, Texas.

Screening Visit

Screening consisted of consent, medical history, physical examination, SPT, spirometry, and, when appropriate, a urine pregnancy test.

ACC Screening Exposure (Exposure 1) (Day 1)

Qualifying participants entered the ACC for 3 hours of exposure to RW at a mean (SD) pollen count of 3,500 (700) grains/m^3, a density used for all subsequent ACC exposures. Trained ophthalmic technicians performed staff-rated ocular assessments, including ocular redness and lid swelling, and participants self-assessed ocular itching and tearing at 30-minute intervals. To continue in the study, participants were required to score 2 or greater on staff-assessed ocular redness in at least 1 region (nasal or temporal) in each eye within the 3-hour period of exposure.

Complete Ophthalmic Examination Visit (Days 4–7)

After chamber exposure 1, a complete ophthalmic examination (COE), including Early Treatment Diabetic Retinopathy Study

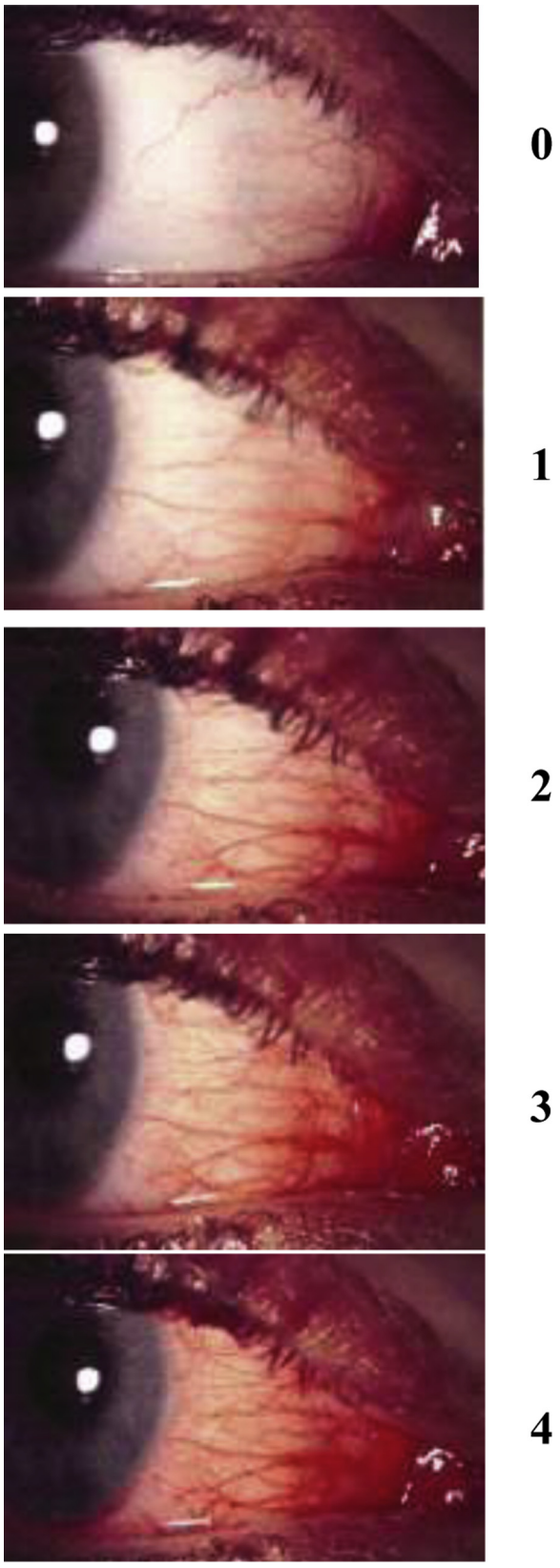

Figure 1. Ocular signs and symptoms assessments. Separate ratings for temporal and nasal regions 1 through 4 in each eye. Modified from the validated bulbar redness 5 scale.