Clinical Validation of Controlled Grass Pollen Challenge in the Environmental Exposure Unit (EEU)

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Abstract

**Rationale:** The Environmental Exposure Unit (EEU), a controlled allergen exposure model of allergic rhinitis (AR), has traditionally utilized ragweed pollen. We sought to clinically validate the use of grass pollen in the EEU.

**Methods:** Healthy volunteers with a history of AR symptoms during grass pollen season and supportive skin test responses attended the EEU for 3hrs of rye grass pollen exposure (Lolium Perenne). Non-atopic controls were also recruited. Subjects exposed individual rhinoconjunctivitis symptoms to generate Total Nasal Symptom Score (TSS) and/or Pollen Nasal Index (PNIF) values. Two separate groups allowed for the exploration of lower vs. higher pollen concentrations and subsequent effects on symptoms.

**Results:** 78 subjects were screened, of whom 39 were eligible and attended the 2x3hr EEU visits, plus 8 non-atopic controls. Mean TSS, TNSS and PNIF values amongst participants in the higher pollen concentration group (target 3500 grains/m³) after the first 3 hour exposure were 18.9, 9.7 and 68, respectively. In comparison, mean TSS, TNSS and PNIF values in the lower pollen concentration (2500 grains/m³) group were only 13.3, 7.6 and 33, respectively. The subacute phase of pollen exposure did not appreciably alter the maximal TSS/TNSSs, but rather resulted in a more rapid onset of symptomatology, with higher TNSS and PNIF values in the lower pollen concentration (2500 grains/m³).

**Conclusions:** This study provides clinical validation of the ability to generate allergic rhinoconjunctivitis symptoms amongst grass-allergic individuals in the EEU.

Methods

- Participants on file from previous enrolment in an EEU study were approached to participate.
- Healthy males or females between the ages of 18 and 65 with a positive skin prick test to grass allergen and at least a two year history of seasonal allergic rhinitis symptoms during the grass pollen season were non-atomatic and able to abstain from the use of restricted medications (See Table 1) were eligible to participate. 8 Non-atopic healthy controls were also included to confirm a lack of clinical reactivity among non-grass allergic individuals.
- After providing written consent, participants underwent the following procedures at screening: vital signs, skin testing to a panel of allergens (including rye grass), height & weight, physical examination including detailed nasal examination, and urine pregnancy testing (women of childbearing potential).
- Participants recorded their allergic rhinitis symptoms of runny nose, nasal congestion, sneezing, nasal itching, red/burning eyes, itchy eyes, watery eyes and itching of the ears/palate/throat (Table 2), and peak nasal inspiratory flow measurements every half hour during the 3 hour pollen exposure sessions, and for the ensuing 9 hours (12 hours total) after the first of the two sessions to document late phase reactions.

Results

- Eligible participants attended two back to back 3 hour grass pollen exposure visits in the EEU. Prior to entering the EEU, participants were reviewed for medication and adverse events to ensure eligibility was still met, and peripheral blood was collected for biomarker analysis.
- Participants recorded their allergic rhinitis symptoms of runny nose, nasal congestion, sneezing, nasal itching, red/burning eyes, itchy eyes, watery eyes and itching of the ears/palate/throat (Table 2), and peak nasal inspiratory flow measurements every half hour during the 3 hour pollen exposure sessions, and for the ensuing 9 hours (12 hours total) after the first of the two sessions to document late phase reactions.

Discussion

- The EEU has been in operation since the late 1980’s but has heretofore distributed primarily ragweed pollen due to the high local prevalence of ragweed allergy (Day and Briscoe, Ann Allergy Asthma Immunol 1999; 83: 85-93).
- We had validated the dispersal equipment for the delivery of grass pollen, but not clinically validated the allergic rhinitis responses of grass allergic individuals (Walker and Ellis, Ann Allergy Asthma Immunol 2011; 107(5): A9).
- The current study confirms that our grass pollen delivery in the EEU elicits an appropriate clinical response in grass pollen allergic individuals.
- Symptom scores were somewhat lower when we utilized a lower target pollen concentration (2500 grains/m³) correlated well with the participant’s subjective scoring.
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- Peak Nasal Inspiratory Flow (PNIF) measurements correlated well with the participant’s subjective scoring of nasal congestion.

Conclusions

- The EEU has been clinically validated for the study of grass pollen allergic individuals.
- Symptomatic responses to rye grass pollen were in agreement to those seen with ragweed pollen distribution.
- The known cross reactivity between rye grass and other grass pollen types was confirmed clinically via this evaluation as well.