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 assessed individual rhinoconjunctivitis symptoms to generate Total Nasal Symptom Score (TNSS; max 12) and Total Symptom Score (TSS; max 24) and recorded Peak Nasal Inspiratory Flow (PNIF) q30min while in the EEU. Subjects returned the following day for an additional 3hrs of pollen exposure. 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 2x3h EEU visits, plus 8 non-atopic controls. Mean TSS, TNSS and PNIF values amongst participants in the higher pollen concentration group (target 3500 grains/m^3) 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/m^3) group were only 13.3, 7.6, and 82, respectively. The subsequent day of pollen exposure did not appreciably alter the maximal TSS/TNSSs, but rather resulted in a more rapid onset of symptomatology, with higher mean scores at the 30min, 60min and 90min time-points. The non-atopic controls remained asymptomatic.

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

Background

•The Environmental Exposure Unit (EEU) is a unique, internationally recognized research facility that allows for the exposure of groups of 5 to 150 volunteers to ambient levels of airborne allergens such as ragweed pollen. Within this specially designed room located within Kingston General Hospital, allergen levels can be precisely maintained at predetermined levels and environmental variables including air quality, temperature, humidity and CO_2 levels are tightly regulated. With the ability to control these variables, study conditions can be reproduced on different days and at any time of the year, something that cannot be achieved with any other research model for allergic rhinitis.

•Traditionally, studies conducted in the EEU have utilized ragweed pollen exclusively due to the high prevalence of ragweed pollen allergy in Southeastern Ontario. We had previously validated the pollen dispersal equipment for adaptation to grass pollen dispersal.

Objective

To clinically validate the distribution of rye grass pollen in the Environmental Exposure Unit (EEU)

Methods

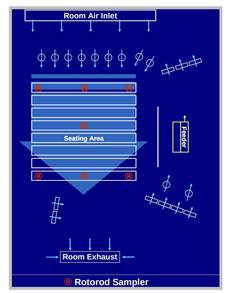
- Participants on file from previous enrolment in an EEU study were approached to participate
- Healthy males or females between the ages of 18 and 65 with a positive skin prick test to grass allergen and at least a two year history of seasonal allergic rhinitis symptoms during the grass pollen season who were non-asthmatic 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 in 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 only)
- 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

Table 1: Medication Washout Periods

Medication	Washout Period
Antihistamines	7 days
Intranasal or inhaled corticosteroids	14 days
Intranasal or inhaled cromolyn	14 days
Systemic corticosteroids or astemizole	30 days

Table 2: Symptom Score Definitions

Rating	Definition
0 = None	Symptom is completely absent
1 = Mild	Symptom is present, but not bothersome
2 = Moderate	Symptom is bothersome, but tolerable
3 = Severe	Symptom is hard to tolerate, desiring treatment



Results

• 78 participants were screened, of whom 39 were eligible and attended the 2x3h EEU visits, plus 8 non-atopic controls

• All subjects with positive skin tests to timothy grass demonstrated positive tests to rye grass as well

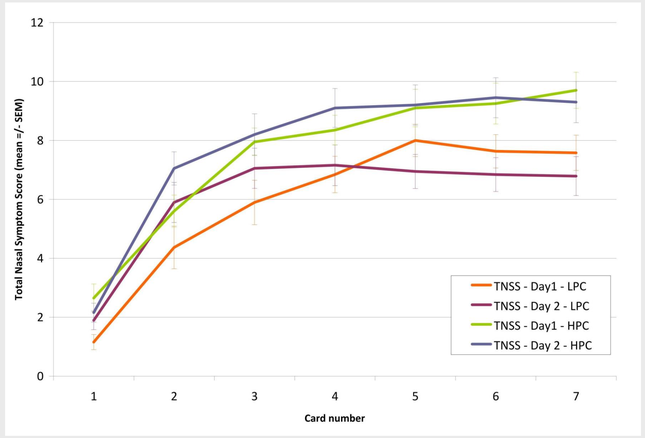
• Mean TSS, TNSS and PNIF values amongst participants in the higher pollen concentration group (target 3500 grains/m^3) after the first 3 hour exposure were 18.9, 9.7 and 68, respectively

• In comparison, mean TSS, TNSS and PNIF values in the lower pollen concentration (2500 grains/m^3) group were only 13.3, 7.6, and 82, respectively

• The subsequent day of pollen exposure did not appreciably alter the maximal TSS/TNSSs, but rather resulted in a more rapid onset of symptomatology, with higher mean scores at the 30min, 60min and 90min time points

• Non-atopic controls remained asymptomatic (data not shown)

Figure 1: Total Nasal Symptom Scores over two consecutive pollen exposure visits: Higher Pollen Concentration (HPC) and Lower Pollen Concentration (LPC)



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: 83-93)

• We had validated the dispersal equipment for the distribution 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/m^3) compared to our historically established 3500 grains/m^3

• The TNSS scores generated from the group exposed to 3500 grains/m^3 of rye grass pollen generally mirrored the responses seen previously with our ragweed pollen exposures, with some individuals reacting quickly with high symptom scores and others to a lesser degree (Ellis et al., Ann Allergy Asthma Immunol 2010; 104: 293-8)

• The second subsequent day of pollen exposure generally produced an earlier peak of symptoms, but not a greater mean TNSS overall

• 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 similar 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

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