Baseline Challenge Responses during Repeated, Daily Controlled Exposures to Grass Pollen in the Environmental Exposure Unit (EEU)

Ellis AK, MD MSc FRCPC FAAAAI[1, 2], Steacy LM, BSc[1], Walker T, BA[1], Hobsbawn B[1]

1 – Allergy Research Unit, Kingston General Hospital, Kingston, ON Canada, 2 – Department of Medicine, Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON Canada

Abstract

Background/Rationale: The Environmental Exposure Unit (EEU), a validated model of allergic rhinitis(AR), has recently been adapted for grass pollen distribution. We report AR responses to multiple consecutive daily exposures to grass pollen.

Methods: Healthy volunteers with a history of AR symptoms during grass pollen season and supportive skin test responses attended the EEU for four consecutive (daily) 3hr rye grass pollen exposure sessions. Participants assessed individual rhinoconjunctivitis symptoms to generate a Total Nasal Symptom Score (TNSS; max 12) and Total Rhinoconjunctivitis Symptom Score (TRSS; max 24) and recorded Peak Nasal Inspiratory Flow (PNIF) q30min in the EEU. Participants who did not achieve the minimum symptom requirement of a TRSS of at least 10 and a TNSS of at least 6 on any card on the 3rd exposure visit were excluded and did not attend the 4th challenge.

Results: 348 participants were screened, of whom 214 were eligible and attended all 3 of the first 3 x 3hr EEU visits. Mean TRSS and TNSS scores amongst participants after the first 3hr exposure were 13 and 7, respectively. On the conclusion of Day 2, these values were 15, and 8; following Day 3 they were 17, and 8. 17 participants did not meet the required TRSS/TNSS scores on Day 3 and were excluded at that point. Final mean TRSS and TNSS concluding Day 4 were 18 and 9; one participant did not re-qualify on Day 4.

Conclusions: This study characterized the generation of allergic rhinoconjunctivitis symptoms amongst grass-allergic individuals over repeated daily exposures 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 and grass 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 a priming session design involving a minimum of 1 but a maximum of 5 exposure sessions. Upon achieving the required symptom scoring the participants were not required to return for further pollen exposure visits. A recent clinical trial required 4 consecutive and mandatory pollen exposure visits.
- We thus had a unique opportunity to study trends in symptom development compared to our traditional model.

Objective

To describe the pattern of symptomatic responses following four consecutive pollen exposure visits, and to determine if such a protocol enhances the ability for potential study qualification compared to a priming model.

Methods

- Healthy males or females between the ages of 18 and 65 with a positive skin prick test to rye grass allergen and at least a two year history of seasonal allergic rhinitis symptoms during the grass pollen season and who were non-asthmatic were eligible to participate.
- Participants were excluded if they had a previous history of asthma (greater than GINA step 1); a history of anaphylaxis to grass allergen; FEV_1 < 80% predicted; had received immunotherapy within 12 months or had any history of grass immunotherapy within 10 years; received treatment with beta blockers; were unable to receive epinephrine (i.e severe hypertension); history of recurrent acute or chronic sinusitis and significant drug or alcohol abuse.
- 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, routine blood and urine testing (including pregnancy testing for women of childbearing potential) and spirometry.

Table 1: Symptom Score Definitions and List of Symptoms

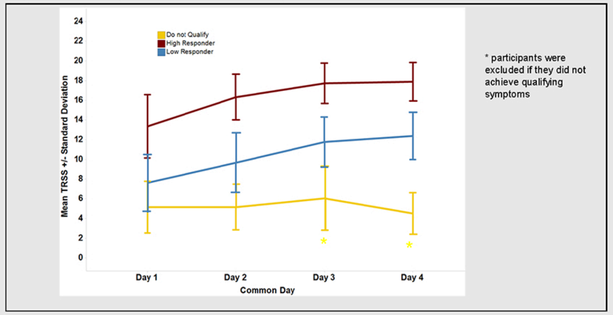
Rating	Definition	Symptoms	
0 = None	Symptom is completely absent	Running Nose	Itchy Eyes
1 = Mild	Symptom is present, but not bothersom	Sneezing	Watery Eyes
2 = Moderate	Symptom is bothersome, but tolerable	Blocked Nose	Red/Burning Eyes
3 = Severe	Symptom is hard to tolerate, desiring treatment	Itchy Nose	Itching of Ears, Palate or Throat

- Eligible participants attended four consecutive 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. Participants had their vital signs and Peak Expiratory Flow (PEFR) measured both before and after pollen exposure.
- 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 1), and peak nasal inspiratory flow measurements every half hour during the 3 hour pollen exposure sessions.
- Participants were required to achieve a TRSS of at least 10 and a TNSS of at least 6 on any card during both the 3rd and 4th exposure sessions.

Results

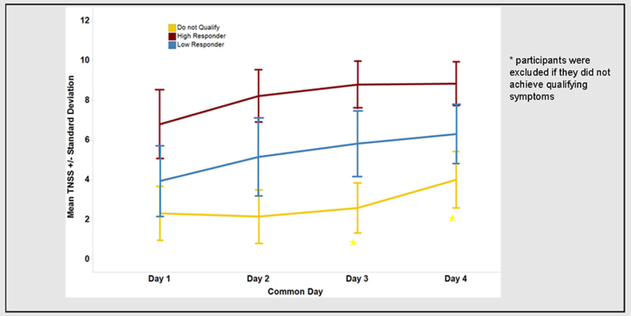
- A total of 348 participants were screened, of which 214 were eligible and attended the first 3 EEU pollen exposure visits.
- The participants who qualified were split into 2 groups for this sub-study; high and low responders. High and low responders achieved an average TRSS ≥ 14 and < 14 respectively over the course of the four baseline challenge visits.
- Many low responders did require at least 2 days of exposure to obtain qualifying symptoms but once these were achieved they were maintained on the subsequent days (Figure 1).

Figure 1: Mean Total Rhinoconjuctivitis Symptom Scores over four consecutive pollen exposure visits (+/- standard deviation).



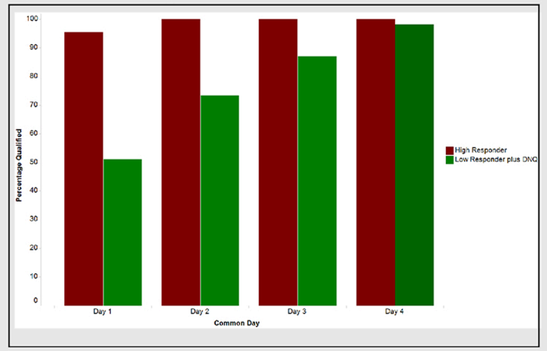
- Participants with very low TRSS and TNSS scores on Day 1 did not obtain the qualifying scores required on any subsequent day (Figures 1 and 2).
- The majority of high responders (96%) qualified after the first day and 100% after Day 2; these symptoms were reproducible on Days 3 and 4 (Figure 3).
- 1 participant withdrew due to intolerable symptoms after Day 1 and 1 participant withdrew due to a schedule conflict after Day 1.
- PNIF measurements correlated well with increasing in nasal congestion.

Figure 2: Mean Total Nasal Symptom Scores over four consecutive pollen exposure visits (+/- standard deviation).



Results (cont'd)

Figure 3: Percentage Qualified after each pollen exposure visit.



Discussion

- The EEU has been in operation since the late 1980's but has primarily distributed ragweed pollen due to the high local prevalence of ragweed allergy (Day and Briscoe, Ann Allergy Asthma Immunol 1999; 83: 83-93)
- We have validated the dispersal equipment for the distribution of grass pollen (Walker and Ellis, Ann Allergy Asthma Immunol 2011; 107(5): A9) and the allergic rhinitis responses of grass allergic individuals (Ellis et al., Ann Allergy Asthma Immunol 2010; 104: 293-8)
- The current study suggests that the traditional priming design would be the preferable method as it allows the sessions to adapt to the individual needs of the participant instead of the group as a whole. With a priming design the high responders can leave the EEU upon achieving the required symptoms to prevent unnecessary exacerbation of their allergy symptoms.

Conclusions

- High responders are able to maintain their qualifying symptoms suggesting that repeated pollen exposure visits after the participants qualify are unnecessary.
- Low responders do appear to require multiple days to qualify but once they reach the required level of symptoms they are reproducible each subsequent day.
- Participants who exhibit little to no symptoms on Day 1 are unlikely to obtain qualifying scores after repeated exposure sessions.

This study was funded by Circassia Ltd and Adiga Life Sciences Ltd.