Factors Affecting the Allergic Response to Ragweed Allergen Challenge

Ellis AK, Ratz JD, Day A, Rafeiro E, Day JH

Division of Allergy & Immunology, Queen's University and Kingston General Hospital, Kingston, ON, Canada

Abstract

Rationale: Persons with seasonal allergic rhinitis (SAR) respond to allergen re-exposure differently. This study was designed to determine influences on rate and degree of symptom development to controlled ragweed pollen exposure.

Methods: Demographics, recent exposure history to household allergens and irritants, as well as Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) data were obtained from ragweed-allergic subjects who also underwent skin prick testing to selected aeroallergens. Nasal eosinophils were counted. Subjects returned for 3-hour ragweed pollen exposure in the Environmental Exposure Unit (EEU) where a Total Symptom Score (TSS) curve was generated by rating rhinoconjunctivitis symptoms q30 min. A mixed-effects model compared TSS curves between baseline factors.

Results: 123 subjects completed the study. Skin test reactivity to ragweed did not correlate with TSS curve generation. Significant associations occurred between TSS curves and positive skin test reactivity to dust mite, dog, cat and grass, as well as subject self-report of symptoms upon dog, cat, and other animal exposure. Visual analogue scale ratings of SAR symptoms during both ragweed and grass seasons and RQLQ scores were also positively associated with TSS curves. No other associations were detected.

Conclusion: This study indicates a relationship between the rate and degree of symptom development to controlled ragweed exposure and immediate skin test reactivity to dust mite, animals, and grass pollen. Symptom development also correlated with self-reported symptoms to animals, seasonal grass and ragweed exposure, as well as rhinitis-specific quality of life. No associations were shown with late-phase response, nasal eosinophils or degree of skin test reactivity to ragweed.

This study was self-funded.

Introduction

- Seasonal allergic rhinitis (SAR), particularly ragweed allergy, is prevalent in North America
- Symptoms of ragweed allergy are variable in degree between allergic individuals
- Anecdotal evidence indicates a non-linear relationship of symptoms to skin prick test results
- Factors that affect symptom development are not well characterized
- The Environmental Exposure Unit (EEU) is a model of controlled allergen challenge
- Symptoms developed in the EEU similar to those experienced in ragweed season
- EEU has been validated for evaluating anti-allergic medications
- "Priming" of the allergic response is an essential phase of EEU study design
- Question remains as to why some subjects prime quickly and others more slowly

Objective

- This study aimed to determine factors responsible for clinical response to controlled ragweed pollen exposure in sensitized subjects

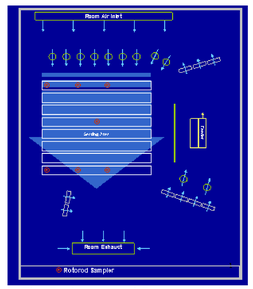
Methods

***Inclusion Criteria*:**
- Males or females aged 16 to 70
- Documented positive skin test to ragweed (wheal ≥ 3mm)

***Exclusion Criteria*:**
- Unwilling or unable to observe washout periods for specified medications
- Upper respiratory tract infection
- Asthma requiring more than occasional short-acting beta-agonist treatment

Baseline Evaluation (Screening):
- Medication/medical history and nasal exam performed by study physician
- Skin prick testing to the following allergens:
  - short ragweed
  - mixed ragweed
  - *Aspergillus*
  - *Alternaria*
  - *Penicillium*
  - *Hormodendrum*
  - *D. Pteronyssinus* (dust mite)
  - *D. farinae* (dust mite)
  - dog hair
  - cat pelt
  - mixed grass
  - mixed trees
- Questionnaire package completed for demographic data, self-report of hayfever season symptomatology, other allergic history (food, drugs), exposure history to other allergens/irritants, QOL scales [RQLQ (disease specific) & SF36 (non-disease specific)]
- Nasal smears for eosinophilia
- Subject measured the presence and size of late phase reactivity at 8-12 hours

Pollen Exposure:
- Subjects attended one 3-hour session of short ragweed pollen exposure in the EEU
- Symptoms were recorded on diary cards at the beginning of the session, and every half-hour
- Study physicians monitored subjects during the pollen exposure period



The Environmental Exposure Unit: Graphical Layout

Symptom evaluation:

Subjects rated symptoms of:
- runny nose
- sneezing
- itchy nose/palate/throat

According to scale of:
0 = None
1 = Mild (Symptom present, but not bothersome)
2 = Moderate (Symptom bothersome, but tolerable)
3 = Severe (Symptom hard to tolerate, desiring treatment)

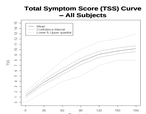
Scores were summed to generate a Total Symptom Score (**TSS**)

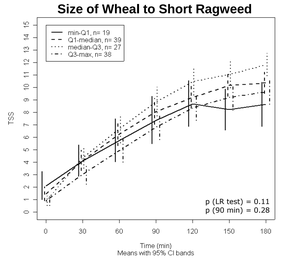
Statistical Analysis:

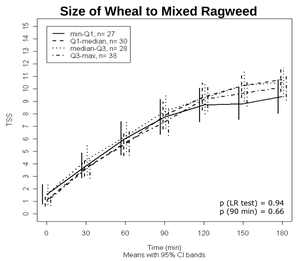
The TSS curves were modeled by a second order polynomial. A mixed effects regression model with unstructured within-subject correlation was used to account for the dependence induced by the repeated measures design. Likelihood ratio (LR) tests with three degrees of freedom were used to compare the overall shape (intercept, slope and curvature) of the curves between groups. In addition, the model was used to compare the expected difference between groups at 90 minutes. Estimates were calculated by restricted maximum likelihood as implemented in the SAS V8.2 *MIXED* procedure.

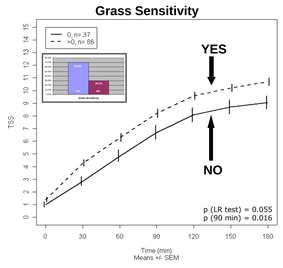
Results

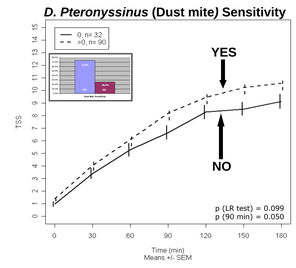
- 140 subjects screened, 123 qualified and attended the 3-hour pollen exposure session
- mean age of subjects was 37 (range 16-69)
- 76 (61.8%) were female

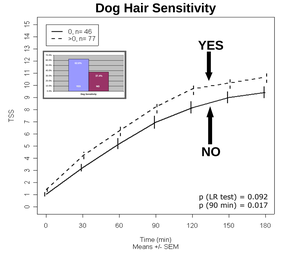


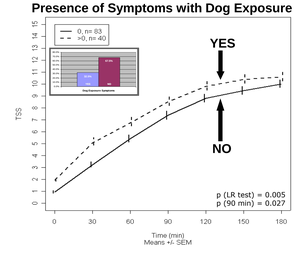


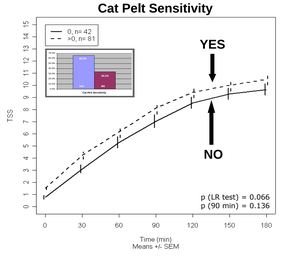


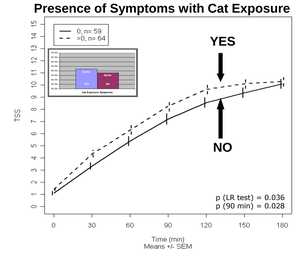




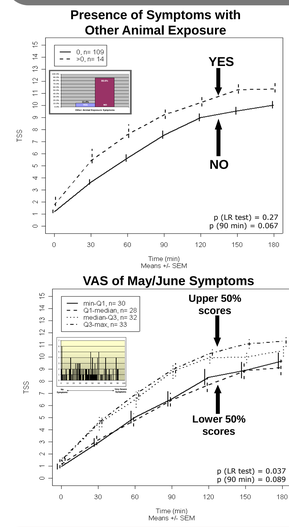


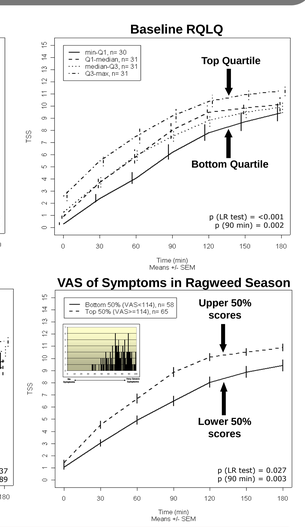






Results - con't





Results Summary

Present study indicates SAR symptom development is increased by priming effect of perennial allergens and multiple allergen sensitivity, specifically:
- Dust mite, dog, cat and grass sensitivity showed trends towards increased rate and degree of symptom development on ragweed exposure
- Self-report of dog, cat, grass and ragweed exposure were associated with increased rate and degree of symptom development on ragweed exposure
- Poorer rhinitis-specific Quality of Life (RQLQ) was associated with an increased rate and degree of symptom development
- There was a lack of correlation between ragweed skin test reactivity (both short and mixed) and the level of allergic symptoms
- Absent relationship of symptom development with irritant exposure (smoke, paint fumes), nasal eosinophils, late phase response to all allergens tested or drug/food allergy
- No correlations observed between level of allergic symptoms and sensitivity to mixed trees, molds or fungi nor the SF36 questionnaire

Conclusions

Allergic symptoms to ragweed are:

Increased by:
- **concomitant sensitivity and exposure to perennial allergens (dust mite, dog, cat) and grass pollen**

Unaffected by:
- **degree of skin test reactivity to ragweed, irritant exposure, late-phase responses or nasal eosinophils**

Rate of development and symptom severity increased with poorer rhinitis-specific Quality of Life (RQLQ)