

Controlled allergen challenge clinical trials: Impact upon allergy season symptoms?



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Abstract

Introduction: The Environmental Exposure Unit (EEU), which uses controlled allergen exposure, is a validated model of allergic rhinitis (AR). The impact on seasonal reactivity over time in subjects who participate in EEU trials has yet to be assessed. The objective of this study was to assess the effect, if any, on subsequent seasonal AR symptoms in subjects that participated in multiple EEU studies during a 3 year period.

Methods: An initial Ragweed Season Survey (RWSS) was mailed to 1821 ragweed-allergic individuals in our database during the third week of the 2003 ragweed season, documenting the nature and severity of their AR symptoms. For the ensuing 3 years (Sept 2003 to April 2006), all EEU trial participants were invited to complete a similar questionnaire and the RWSS was again mailed during ragweed season. The primary outcome of interest was the mean symptom severity scores during ragweed season from year to subsequent year in those subjects participating in multiple EEU trials. Means were compared using the Mann-Whitney test and p-values adjusted for repeated measures. Approval was obtained from the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board and informed consent obtained from all research subjects.

Results: The yearly response rate for completed RWSS and EEU surveys is shown in the table below. Evaluating subjects who completed all RWSSs and all EEU trial questionnaires during the 3 year study period, resulted in a sample of 140 subjects for the primary outcome analysis. Mean symptom severity ratings for nasal, ocular and other AR symptoms for both typical and peak ragweed season days were unchanged from one year to the next in these subjects.

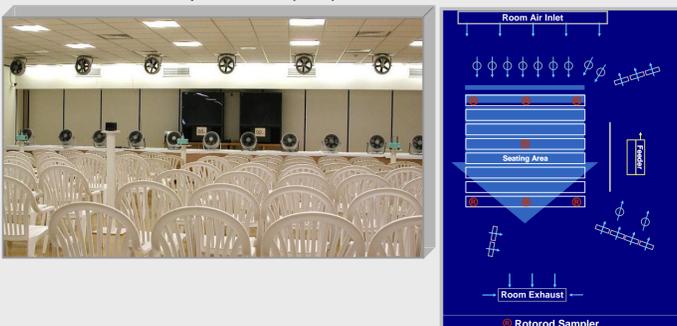
Conclusions: Participation in EEU trials did not affect subjects' subsequent seasonal AR symptoms nor symptoms in EEU trials.

Introduction

Exposure of patients to allergens varies considerably under normal living conditions and allergen levels can affect reported symptom severity. The Environmental Exposure Unit (EEU) in Kingston General Hospital provides a controlled environment in which subjects can be exposed to closely regulated and reproducible levels of a selected allergen and is a validated model for the study of allergic rhinitis.

EEU researchers and others have previously questioned whether or not participation in EEU clinical trials could have an impact on allergic rhinitis symptom severity over time in subjects that undergo pollen exposure in the EEU. In order to address this question, a survey study was undertaken to assess the impact, if any, on subjects' seasonal reactivity by asking subjects to complete questionnaires both during the local ragweed season as well as subsequent participation in EEU clinical trials over a 3 year period.

The Environmental Exposure Unit (EEU)



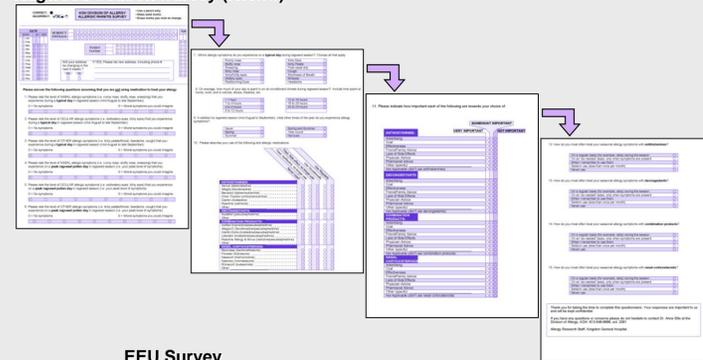
Objective

To assess the effect, if any, on subsequent seasonal AR symptoms in subjects that participated in multiple EEU studies during a 3 year period.

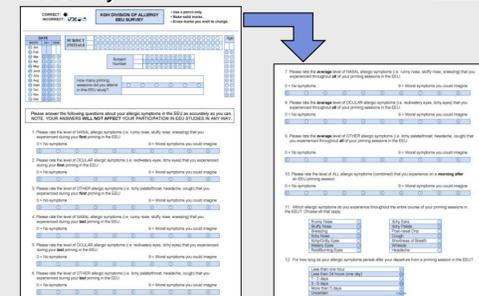
Methods

- Initial Ragweed Season Survey (RWSS) was mailed to 1821 ragweed-allergic individuals in our database during the third week of the 2003 ragweed season, documenting the nature and severity of their AR symptoms
- For the ensuing 3 years (Sept 2003 to April 2006), all EEU trial participants were invited to complete a similar questionnaire and the RWSS was again mailed during ragweed season
- Primary outcome of interest was the mean symptom severity scores during ragweed season from year to subsequent year in those subjects participating in multiple EEU trials
- Only those subjects who completed all three years of RWS surveys and participated in at least one EEU study per year were included in the final dataset for analysis
- Means were compared using the Mann-Whitney test and the Kruskal-Wallis test for non-parametric data.
- Approval was obtained from the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board and informed consent obtained from all research subjects

Ragweed Season Survey (RWSS)



EEU Survey



Results

The yearly response rate for completed RWSS and EEU surveys is shown in the table below. Evaluating subjects who completed all RWSSs and all EEU trial questionnaires during the 3 year study period, resulted in a sample of 140 subjects for the primary outcome analysis.

Year	RWSS	EEU Survey
2003-04	549	516
2004-05	471	331
2005-06	360	418

Ragweed Season Survey (RWSS) Mean Symptom Severity Scores over 3 years (severity scale from 0 to 9)

Symptom	2003	2004	2005	P-value*
Nasal - Typical	6.39	6.18	6.24	0.559
Ocular - Typical	5.84	5.94	5.83	0.805
Other - Typical	5.18	5.24	5.22	0.994
Nasal - Peak	7.94	7.72	7.76	0.127
Ocular - Peak	7.29	7.31	7.22	0.975
Other - Peak	6.57	6.57	6.56	0.957

* Kruskal-Wallis, non-parametric data

EEU Survey Mean Symptom Severity Scores over 3 years (severity scale from 0 to 9)

Symptom	2004	2005†	2006	P-value*
Nasal - First Prime	6.34	7.18	6.68	0.001
Ocular - First Prime	6.32	6.89	6.45	0.182
Other - First Prime	5.58	6.17	5.73	0.248
Nasal - Last Prime	6.56	7.35	6.77	0.002
Ocular - Last Prime	6.52	7.06	6.56	0.276
Other - Last Prime	5.71	6.24	5.65	0.273
Nasal - Ave Prime	6.56	7.23	6.72	0.011
Ocular - Ave Prime	6.61	7.02	6.51	0.221
Other - Ave Prime	5.75	6.19	5.67	0.415

* Kruskal-Wallis, non-parametric data

† all subjects were required to have a minimum nasal symptom score for study entry in the 2005 EEU study whereas the 2004 and 2006 studies did not

Discussion

- Seasonal allergic rhinitis is a dynamic disease and severity of symptoms is known to differ from year to year in patients based on factors such as outdoor pollen counts, concomitant allergen exposures, and individual susceptibility patterns.
- Concern has been raised that repeated participation in allergen challenge trials such as those conducted in the EEU could lead to an ongoing 'permanent priming' phenomenon, whereby in-season symptoms would become more severe over time as more exposure studies were completed by subjects.
- This evaluation did not demonstrate any changes in ragweed symptom severity over the course of three years of study in subjects participating in yearly EEU trials.
- Specifically, mean symptom severity ratings for nasal, ocular and other AR symptoms for both typical and peak ragweed season days were unchanged from one year to the next in these subjects.
- The 2005 EEU study required a minimum nasal symptom score and a higher baseline total symptom scores for study entry. This translated into subjects perceiving and recording higher mean symptom severity scores on the EEU survey in that year compared to others. Despite the higher level of symptoms required for EEU study participation in 2005, subject symptoms in the ensuing ragweed season were not different compared to previous years.
- Despite higher symptom scores in the 2005 EEU study, symptoms scores in the subsequent 2006 EEU study that did not include a minimum nasal symptom score requirement were not different compared to symptom scores in the 2004 EEU study.

Conclusions

- **Participation in multiple EEU trials does not impact upon the severity of in-season AR symptoms experienced by EEU subjects**
- **Symptom severity experienced by subjects participating in EEU trials is a function of the particular study protocol, and not affected by participation in multiple studies**

