Ocular Allergen Exposure: A Naturalistic Environmental Exposure Chamber Model versus a Direct Instillation Model

#P86

Maria J. Tort,[1] Richard Ornberg,[1] Bruno Lay,[2] Fiona Soong,[3] Anne Marie Salapatek[3]

[1] Alcon Research Ltd, Fort Worth, TX, USA

[2] ADCIS, Saint-Contest, France

[3] Cetero Research, Mississauga, ON, Canada

Abstract

Introduction: While direct-instillation models are useful for evoking allergic responses, direct instillation does not mimic everyday exposures to allergens. This study compared a direct-instillation ocular allergen exposure model to a more naturalistic airborne allergen exposure model.

Methods: Thirteen subjects with a history of ragweed allergy and a positive skin prick response attended screening, dose-finding, dose-confirmation, and analysis study visits. For conjunctival allergen provocation testing (CAPT), 1 drop of ragweed allergen was administered to each eye, at the lowest possible subject-specific concentration between 1.6 and 100 protein nitrogen units per 25 µl drop. For environmental exposure chamber (EEC) testing, subjects were exposed to continual airborne ragweed pollen at 3500 ± 500 particles/m^3. Itching was assessed on diary cards by subjects, and hyperemia was assessed by clinicians, using standardized 9-point scales from 0 (none) to 4 (extremely severe) in 0.5-unit increments. Assessment time points (for itching assessment and hyperemia grading) were 30 and 0 minutes before exposure (via CAPT or EEC), and 15, 30, 60, 90, 120, 150, and 180 minutes after exposure. The CAPT included additional hyperemia assessments at 5, 10, and 20 minutes after exposure.

Results: Mean baseline hyperemia was <1 unit ("mild") and mean baseline itching was <0.5 units for both CAPT and EEC analyses. With CAPT, hyperemia spiked quickly at 30 minutes after exposure, reaching a maximum hyperemia of 2.3 ± 0.6 units (between moderate and severe hyperemia), and decreasing at subsequent time points. With EEC testing, the hyperemia increased gradually, reaching a maximum of 1.9 ± 0.5 units (approximately moderate hyperemia) at 180 minutes, which was the end of the observation period. With CAPT, itching spiked at 20 minutes after exposure, reaching a maximum itching of 2.8 ± 1.0 units, and decreasing thereafter. With EEC, the itching increased gradually, reached a maximum of 2.8 ± 1.0 units at 180 minutes after exposure, and appeared to be still increasing.

Conclusions: The time courses of allergic responses differed between CAPT and EEC models; however, both models evoked a similar level of sensitivity to allergen exposure. The EEC was a useful challenge model for mimicking airborne allergen exposures that evoke significant ocular responses.

Background

- **Environmental Exposure Chamber (EEC)** testing
  - mimics a natural allergen environment and a typical exposure experience; however, unlike nature, the EEC provides control over the variables that affect allergy sufferers
  - delivers a level of allergen exposure that can maximize a patient's clinical response; this has facilitated research into the therapeutic effects of systemic, nasal, and ophthalmic anti-allergy medications[1]
  - has had an important role in the evaluation of allergic rhinitis[1]
  - has also been used to study allergic conjunctivitis[1]
- **Conjunctival Allergen Provocation Testing (CAPT)**
  - has had an important role in the evaluation of allergic conjunctivitis, and has been a mainstay for testing ophthalmic anti-allergy medications[2]
  - uses a concentrated liquid allergen that is instilled directly into the eye in a manner that is not similar to natural allergen environments

Purpose

This study was designed to compare CAPT versus EEC testing for the evaluation of the signs and symptoms of allergic conjunctivitis.

Methods: Subjects and Outcomes Assessment

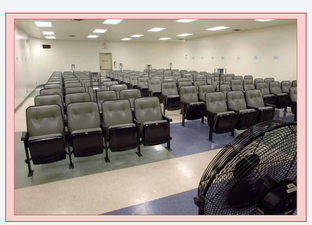
- **Subjects** (n = 13) in good general health who had a history of allergic conjunctivitis and a positive skin prick response to ragweed allergen participated in the study.
- **Signs and symptoms** were assessed on scales from 0 to 4 in 0.5-unit increments
  - Ocular itching for each eye was assessed by subjects using diary cards
  - Hyperemia was assessed by trained staff, who graded nasal & temporal conjunctivae separately in both eyes, using a validated photographic scale[3] for reference

Score	Itching Description	Hyperemia Description
0	None	None / normal
0.5		
1	Tickling sensation involving one or more corners of eye	Mild
1.5		
2	All over tickling sensation	Moderate
2.5		
3	Moderate continuous itching with desire to rub	Severe
3.5		
4	Severe itching with irresistible urge to rub	Extremely severe

- **Analyses** for this interim assessment were as follows:
  - For itching: results for each time point
    - were averaged per subject (left and right eyes) and then per group of subjects (n = 13), and were presented in the abstract as mean ± standard deviation
    - were averaged for all eyes (n = 26) and are presented in the poster as mean ± standard error
  - For hyperemia: results for each time point
    - were averaged per eye (nasal and temporal conjunctivae), then per subject (left and right eyes), then per group of subjects (n = 13), and were presented in the abstract as mean ± standard deviation
    - were selected for worst region (nasal or temporal conjunctiva), then were averaged for all eyes (n = 26), and are presented in the poster as mean ± standard error

Methods: Allergen Exposure Conditions

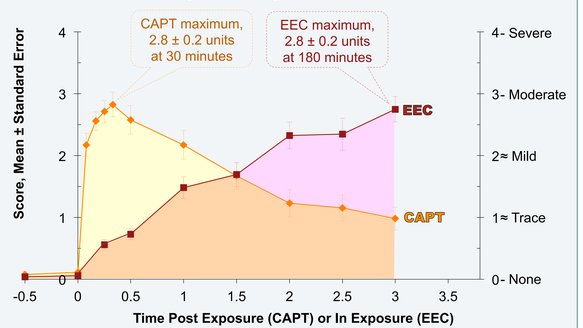
- **EEC conditions**
  - The EEC was validated to show spatial and temporal uniformity of maintaining 3500 ± 500 airborne ragweed pollen grains per cubic meter during the 3 hours that subjects were in the EEC
  - In order to continue to the CAPT phase of the study, subjects were required to respond to the EEC with a score of ≥2 for itching and ≥2 for hyperemia



- **CAPT conditions**
  - A dose-finding visit was conducted ≥7 days before further testing: for each subject, a dose was identified that would elicit a score of ≥2 for itching and ≥3 for hyperemia
    - One drop of diluted ragweed allergen was administered as 1.6 protein nitrogen units per 25 µl in the conjunctival sac; response was assessed 15 minutes later
    - If the initial concentration did not elicit a sufficient response, escalating concentrations were administered approximately every 15 minutes until a sufficient response was observed or until the maximum dose (100 protein nitrogen units / 25 µl) was reached
  - At the next visit, 1 drop of ragweed allergen was administered to each eye, at the previously identified subject-specific provocative concentration; the results from these tests are presented in this poster

Results: Itching Scores Over Time

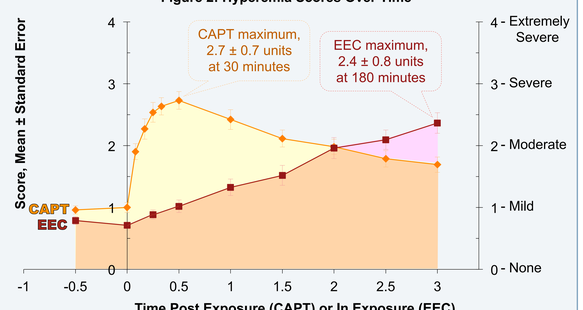
Figure 1: Itching Scores Over Time



- **Before exposure,** itching scores were low and similar between CAPT and EEC conditions
- **After exposure,** the EEC and CAPT conditions induced different allergen response profiles but similar maximum itching scores, representing approximately moderate itching
  - With EEC, the increase in itching was gradual, and itching scores appeared to still be increasing at the end of the observation period with continual allergen exposure
  - With CAPT, the itching scores peaked quickly after allergen instillation and began decreasing after 30 minutes, as allergen began to be cleared from the eyes

Results: Hyperemia Scores Over Time

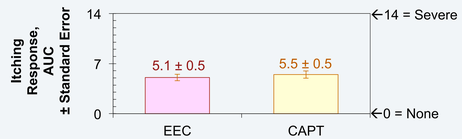
Figure 2: Hyperemia Scores Over Time



- **Before exposure,** mean hyperemia scores were approximately mild or lower, and were slightly higher with CAPT than with EEC testing
- **After exposure,** the EEC and CAPT conditions induced different exposure profiles but similar maximum hyperemia, representing approximately moderate-severe hyperemia
  - With EEC, the increase in hyperemia was gradual, and hyperemia appeared to still be increasing at the end of the observation period with continual allergen exposure
  - After CAPT instillation, the hyperemia scores peaked quickly and to a slightly higher level than the EEC level, and began decreasing slowly after 30 minutes, as allergen began to be cleared from the eyes

Results: Itching Response, Area Under the Curve

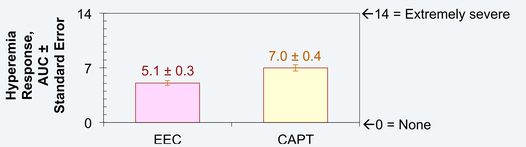
Figure 3: Itching Response, Area Under the Curve (AUC)



For itching response, the areas under the curves were similar for EEC and CAPT exposures.

Results: Hyperemia Response, Area Under the Curve

Figure 4: Hyperemia Response, Area Under the Curve (AUC)



For hyperemia response, the area under the curve was slightly larger with CAPT than with EEC allergen exposures. The difference appeared to be due to the CAPT plot features (Figure 2) of slightly elevated (versus EEC) prechallenge hyperemia, slightly higher (versus EEC) peak hyperemia, and slow decline of postpeak hyperemia.

Discussion and Conclusions

- The time courses of allergic responses differed between CAPT and EEC models; however, both models evoked a similar level of sensitivity to allergen exposure
- Longer than 3 hours of EEC testing might be required to observe maximum allergen-induced ocular itching and hyperemia, but 3 hours was sufficient to elicit a response with EEC that was similar to the response elicited by CAPT
- The two models had different relative advantages and drawbacks:
  - Signs and symptoms were evoked more quickly by the CAPT than by the EEC
  - The EEC was better than the CAPT at mimicking everyday airborne allergen exposures that elicit ocular responses
  - The EEC allowed simultaneous allergen exposure to multiple subjects at once, unlike the one-on-one (investigator-to-subject) CAPT model
  - The EEC testing was conducted in a single visit, while the CAPT required an additional visit to find subject-specific concentrations of allergen
- Ongoing work will study these EEC versus CAPT models for the evaluation of ophthalmic anti-allergy medications

References and Disclosures

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