Development of an Objective Assessment of Conjunctival Hyperemia Elicited via Conjunctival Allergen Provocation Testing (CAPT) and Environmental Exposure Chamber (EEC) Testing

M. Tort[1], R. Ornberg[1], B. Lay[2], R. Danno[2], F. Soong[3], A. Salapatek[3]
[1]Alcon , Fort Worth, TX; [2]ADCIS, Saint-Contest, France; [3]Cetero Research, Mississauga, ON, Canada

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ABSTRACT

Purpose: Conjunctival hyperemia is an important endpoint in ophthalmic clinical research. Most methods for assessing hyperemia are highly subjective and variable across sites. This study describes an imaging method and software system that objectively and automatically quantifies conjunctival hyperemia elicited by ocular allergen exposure.

Methods: Thirteen subjects with a history of allergic conjunctivitis were exposed to ragweed allergen via conjunctival allergen provocation testing (CAPT) and environmental exposure chamber (EEC) testing. Itching was assessed on diary cards by subjects. Hyperemia was assessed by clinicians, using standardized 9-point scales from 0 (none) to 4 (extremely severe). Slit-lamp images of conjunctivae were captured. The Imaging System for Ocular Surface (ISOS; Novartis) was developed as a software suite for automated image analysis of conjunctival blood vessel morphology and redness.

Results: With CAPT, hyperemia transiently rose with a peak at 30 minutes post exposure. With EEC, hyperemia increased gradually, with a maximum at the last time point (180 minutes). Itching scores paralleled the hyperemia scores. Automated image measurements by ISOS provided a variety of vessel morphological measures that were not evident to a clinical observer, including, vessel diameter, total vessel length, vessel density (vessel area/total area, VD), tortuosity, bifurcation points, and dens itometry measurements. Vessel density closely correlated with manual grading captured by trained clinicians for hyperemia assessment. After CAPT instillation, mean VD transiently rose in the initial time points (5, 10 and 20 minutes after exposure) and decreased after 30 min. With EEC, the mean VD increase was gradual, appearing to still be high at the end of the observation period.

Conclusion: Results from this pilot study indicated that the ISOS imaging method and image analysis suite may objectively measure parameters of conjunctival hyperemia resulting from either CAPT or EEC testing.

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INTRODUCTION

- Conjunctival hyperemia is an important endpoint in ophthalmic research that is commonly seen in clinical settings.[1]
- Assessment of hyperemia can be highly subjective and variable across sites.[2,3]
- Objective methods to assess hyperemia have been researched in an effort to develop standardized and reliable techniques.[4,5]
- Allergen provocation models are used to aid in the development of treatments by eliciting allergy signs and symptoms.[6]
- The conjunctival allergen provocation testing (CAPT) and environmental exposure chamber (EEC) models were used in this study.
- In the EEC model, subjects were exposed to controlled and consistent level of natural airborne allergen at levels they would encounter on a typical peak pollen day.
- In the CAPT model, the allergen was directly and repeatedly applied in increasing amounts to the ocular surface until a robust allergic response was elicited.

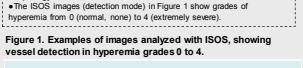
PURPOSE

This study describes an imaging method and software system developed to objectively and automatically quantify conjunctival hyperemia elicited by ocular allergen exposure in two different allergen provocation models.

METHODS AND MATERIALS

- Thirteen ragweed-allergic subjects
- The study population consisted of 7 male and 6 female subjects, between the ages of 28-58 years.
- Environmental Exposure Chamber (EEC) model:
  - ragweed exposure was airborne and continual (3500 particles/m³ for 3 hours)
- Conjunctival Allergen Provocation Testing (CAPT):
  - 1 drop allergen was instilled per eye at subject-specific concentrations
- On scales from 0 (none) to 4 (extremely severe) in 0.5 unit increments, subjects assessed itching and clinicians assessed hyperemia.
- Slit-lamp images of conjunctiva were captured.
- Imaging System for Ocular Surface (ISOS; Novartis) was developed as a software suite for automated image analysis of conjunctival blood vessel morphology.
- The ISOS images (detection mode) in Figure 1 show grades of hyperemia from 0 (normal, none) to 4 (extremely severe).

Figure 1. Examples of images analyzed with ISOS, showing vessel detection in hyperemia grades 0 to 4.



RESULTS

Figure 2. Staff-assessed hyperemia

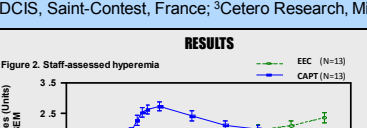


Figure 3. Subject-assessed ocular itching

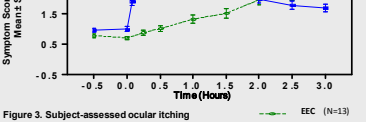
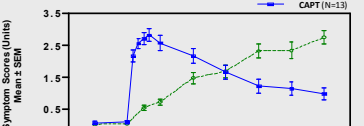


Figure 4. ISOS analysis: mean vessel density



RESULTS

- With CAPT, hyperemia transiently rose with a peak at 30 minutes post-exposure; whereas, in the EEC, hyperemia increased gradually, with a maximum at the last time point (180 minutes) (Figure 1).
- Likewise, the itching curves with CAPT depict a peak at 30 minutes post-exposure; whereas, with EEC, itching increased gradually with the maximum at the last time point (180 minutes) (Figure 2).
- Automated image measurements by ISOS provided a variety of vessel morphological measures that were not evident to a clinical observer, including, vessel diameter, total vessel length, vessel density (vessel area/total area, VD), tortuosity and bifurcation points.
- Vessel density closely correlated with manual grading captured by trained clinicians for hyperemia assessment.
- After CAPT instillation, mean VD transiently rose in the initial time points (5, 10 and 20 minutes after exposure) and decreased after 30 minutes. With EEC, the mean VD increase was gradual, appearing to still be high at the end of the observation period (Figure 2).

CONCLUSIONS

- Both models elicited robust allergic responses, each with a unique kinetic profile.
- Automated image measurements by ISOS provided a variety of vessel morphological measures that were not evident to a clinical observer.
- Results from this pilot study indicated that the ISOS imaging method and image analysis suite may objectively measure parameters of conjunctival hyperemia resulting from either CAPT or EEC testing.

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DISCLOSURES

Maria J. Tort is an employee of Alcon, Fort Worth, TX. Otherwise, the authors have no other financial or proprietary interest in any material or method mentioned.

Current affiliation for Fiona Soong is Eyes on Sheppard Optometric Clinic; Toronto, Ontario Canada. Current affiliation for Anne Maria Salapatek is McMaster University, Department of Biology; Hamilton, Ontario, Canada.

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