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Tear Lipid Layer Thickness with Emollient Eye Drops

THE OHIO STATE UNIVERSITY HUMAN SUBJECTS INSTITUTIONAL REVIEW BOARD
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INNOVATION IN VISION AND EYE CARE RESEARCH GROUP (IVERG)

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Tear Lipid Layer Thickness with Emollient Eye Drops

This study will objectively evaluate two FDA approved artificial tear formulations (Allergan, plc) Refresh Optive and Refresh Optive MEGA-3 in subjects with dry eye symptoms and lipid layer thickness - LLT< 65 nm at baseline in a randomized, cross-over (masked subject) design. We seek to objectively evaluate the increase in lipid layer thickness from baseline at 15 minutes and 1, 2 and 4 hours after an eye drop has been instilled.

Korb, et al (Optom Vis Sci, 2005) have previously shown that an emollient eye drop, will increase the lipid layer of the tear film from ~ 75 to 125nm. We successfully confirmed this with our own IRB approved study at OSU in 2015-2016 which has been accepted for publication. In that previous study, using an emollient eye drop a non-emollient eye drop and our interferometric system, we had no adverse events. The eye drops used in this study will be over-the-counter emollient and non-emollient eye drops made by a different manufacturer than the previous studies.

Objective

To measure and compare the increase in lipid layer thickness of the tear film and symptoms in dry eye patients with a deficient lipid layer 15 minutes and 1 hour after the instillation of an emollient eye drop or a non-emollient eye drop. This is a pilot study to help determine sample size in future studies.

Study Overview

This 20 subject pilot, crossover study will test the lipid layer thickness and morphology of two dry eye related products. All subjects will test one product and following a minimum of a 2-day washout, the same subjects will test another product.

The subjects will have a baseline examination and baseline lipid layer imaging using the King-Smith Stroboscopic Video Color Microscope (SVCM). The baseline examination should last 1 ½ hours. If all criteria are met to continue the study, the 1st eye drop exposure visit will be scheduled or may begin immediately as time allows.

For each eye drop exposure and measurement visit, the eye drop will be applied as to not stimulate tearing or nor apply pressure that would express meibum, and then measurements with the SVCM will be made at 15 minutes, and 1 hour. This will be accomplished at one visit lasting 2 hours. Subjects are permitted to leave and return between the 15 minute and later measurement- but will be instructed not to use any eye drops, eye makeup and not to touch or rub their eyes during that time.

It is anticipated that up to 50 subjects may need to be screened to obtain the 20to 30subjects to enter into the study to complete 20 subjects.

Eligibility and Exclusion Criteria

Inclusion criteria:

- Age – at least 30 years
- Good general health (defined by medication use that has not changed within the last month and the absence of medical conditions or treatments that are deemed confounding to the data as determined by the PI)
- Ability to give informed consent
- Willing to spend time for the study; approximately one hour for a screening visit and additional 1 hour- for the study assessments. Study assessment will be conducted over 2 visit days, approximately 2 hours per day.
- Either gender
- Any racial or ethnic origin
- SVCM tear lipid thickness $\leq$ 75 nm

Contact lens wearers must refrain from lens wear for two days, including the day of the baseline visit, before the baseline examination and during the entire study.

Exclusion criteria:

- Use of any ocular prescription medication (such as but not limited to, glaucoma medications, anti-inflammatory eye drops and Restasis) used within 14 days of the screening visit or started prior to the measurement visit(s).
- Currently having punctal plugs inserted in lacrimal puncta
- Current eye disease, infection or inflammation that affects the surface of the eye such as, but not limited to moderate or greater blepharitis and ocular allergy. Clinically significant (active treatment) of blepharitis, Sjogren's disease or other systemic disease that could influence MGD, corneal, conjunctival, or eyelid abnormalities that could influence lipid layer thickness, conjunctivitis of any cause, ocular infection or systemic medication such as diuretics, SSRIs, that could influence tear secretion, or sensitivity to any of the ingredient in the eye drop being tested,
- Past eye surgery, such as, but not limited to, refractive surgery. Subjects who have had cataract removal surgery more than one year ago, but less than 10 years ago may be considered as potential subjects.
- Female subjects may not be pregnant or lactating. (Subject will be asked to self report these conditions.)
- Infectious diseases (for example, hepatitis, tuberculosis) or an immuno-suppressive disease (for example, HIV). (Subjects will be asked to self-report these conditions.)
- Inability to complete the screening and examination

- Inability to provide analyzable data. For example, subjects who cannot keep their eye open during the entire measurement interval (due to early blinking) or provide a readable eye image (due to eyelid laxity) or cannot sit still for 1 minute.

On visit days, to participate in the study, subjects must:

- Refrain from using eye drops/topical medication at least four hours prior to the visit.
- Refrain from eye rubbing prior to and during the assessment and study visit
- Refrain from using eye makeup. If makeup was worn on the screening or measurement day, the subject must remove it at least one hour prior to the study visit appointment.

Adverse Events

All adverse events will be reported to the IRB and study sponsor, by the PI, within one working day. Adverse Events information will be summarized in the annual report to the IRB as well as to the Sponsor at the end of the study. Adverse events will be assessed and determined by Dr. Jennifer Fogt or Dr. Joseph Barr.

Subject Dismissal

Subjects who, after study team member coaching, are not able to provide analyzable data may be dismissed from the study. Analyzable data is, for example, that which is obtained for the entire measurement interval and provides a readable eye image. Data may not be analyzable if, for example, subjects blink at inappropriate times or have eyelid laxity, to name just two causes issues. These issues are usually revealed at the screening assessment visit. Subjects who cannot provide analyzable data will be dismissed for the study. Subjects who do not keep scheduled visits within the required time frame will be dismissed from the study. Study team members will make reasonable efforts to accommodate subjects' schedules.

Monitoring Procedures

Although the investigators are trained in Good Clinical Practice, FDA requirements for testing, and protected health information, the sponsor will perform a site visit and monitor data integrity at the study site at the Ohio State University College of Optometry, 338 W Tenth Ave. Columbus OH 43210. A representative of sponsor will conduct study initiation and routine monitoring of the study to assure that the site personnel understands the study enrollment and reporting requirements, and initial review and evaluation of adverse events. The procedures for monitoring may include providing reports from the site that indicate the current enrollment and projected date of study completion and periodic site visits as needed. The frequency and scope of periodic site visits will be based upon enrollment, adverse event reports and overall assessment of site performance.

The center participating in this study shall maintain a set of study files on site. The content of the study files shall include a list of all subjects enrolled, correspondence related to the conduct of the study, the protocol and any amendments, CRF for each subject enrolled in the study, and a log of all those individuals who treat and follow subjects, complete and/or correct CRF, and any other documents required by the sponsor, Federal regulations or IRB requirements.

Investigator Responsibilities

Clinical investigators are responsible for: 1) ensuring that the study is conducted according to the signed agreement, investigational plan and applicable FDA regulations; 2) protecting the rights, safety, and welfare of subjects under the investigator's care; 3) control of the test article under investigation; 4) ensure that informed consent is obtained.

The Principal Investigator is responsible for the completion, correction and maintenance of patient Case Report Forms, clinical supplies, and other study documents. The investigator must provide adequate time and resources to the study protocol and must be available to the Sponsor and its representatives via telephone, and in person during site visits. The Investigator shall notify the sponsor of any change in the staff assigned to the study project, location of the device or office space utilized, or responsibility to maintain records within 5 working days of the event. Any plans to change the role or responsibility of any clinical investigators associated with the study must be approved by the sponsor, in advance.

The Medical Monitor will review information provided by investigators (or designee) about potential study subjects who otherwise are qualified but fail to meet all eligibility criteria. All protocol deviations require the consent of the Medical Monitor in advance of exposure.

Protocol Violations, Discontinuation

In the event that a member of the study team or a representative of sponsor becomes aware of a protocol violation, the investigator and the reviewing IRB shall be informed by written correspondence within one work day. If protocol violations continue, the sponsor may take disciplinary action, including probation and termination of participation in the study. All disciplinary actions will be shared with the reviewing IRB.

Discontinuation of the Study

The study may be discontinued due to the loss of instrumentation function (there is only one such instrument) or if patient safety is at risk or data integrity can no longer be assured. The sponsor may discontinue enrollment in the study at any time upon written notification to the clinical investigators. In the event the study is discontinued, sponsor will provide explicit written instruction with regard to study follow-up requirements, maintenance of clinical data, and other pertinent information.