

Viral Conjunctivitis Treatment Study

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1) **Protocol Title**

Treatment of Viral Conjunctivitis with Avenova® (0.01% hypochlorous acid)

2) **Objectives**

The objective of this study is to determine the efficacy Avenova® (0.01% hypochlorous acid) in the treatment of viral conjunctivitis. We hypothesize that patients treated with Avenova® will have a quicker resolution of their ocular signs and symptoms of Viral Conjunctivitis compared with artificial tears.

3) **Background**

Avenova® is a proprietary pure hypochlorous acid under a family of skin cleansing products by NovaBay that has been cleared by the FDA as a 510(k) medical device. Many in vitro studies have evaluated the efficacy of hypochlorous acid against microbacterial and viral agents. In ophthalmology, it is commonly used as a lid cleanser in the treatment of blepharitis and meibomian gland dysfunction. It is applied directly to the lid margin and has an excellent skin and ocular safety profile, which includes a lack of ocular irritation on application. (See included supplemental “Material safety data sheet”.)

We propose a study to evaluate the role of Avenova® (0.1% hypochlorous acid) in the treatment of common ocular viral infections.

4) **Inclusion and Exclusion Criteria***

Inclusion:

Patients who present to Bascom Palmer Eye Institute with a clinical diagnosis of viral conjunctivitis will be allowed to participate in the study. Patients with viral conjunctivitis will be diagnosed clinically with symptoms of either unilateral or bilateral conjunctivitis of less than 1 week duration. These diagnoses will then be confirmed with a viral PCR (patients will only be included with a positive PCR retrospectively). These patients will also need to have at least one of the following: 1. follicular conjunctivitis of the inferior tarsal conjunctiva, 2. mucoid discharge, 3. preauricular lymphadenopathy, and/or 4. associated upper respiratory symptoms.

Exclusion:

Patients with a history of allergic conjunctivitis, history of herpetic eye disease, concurrent diagnosis of bacterial conjunctivitis (based off microbiology plating), purulent discharge, intraocular inflammation, or current contact lens use will be excluded from the study.

Immunocompromised / Immunosuppressed patients, patients with HIV, pregnant women, prisoners, or adults who are unable to provide consent will be excluded.

5) **Number of Subjects***

Total number of subjects to be enrolled is 80

6) **Study Endpoints***

The primary endpoint of the study is the resolution of follicular conjunctivitis by clinical examination (no follicles on tarsal conjunctiva) and symptomatic improvement in viral conjunctivitis by questionnaire.

7) **Procedures Involved***

Patients will be diagnosed by clinical exam in the Bascom Palmer Emergency Department. Those meeting inclusion criteria will be randomized to Avenova® spray vs artificial tears (placebo), to be used in the affected eye four times a day for two weeks duration in total.

The dispensing provider (of the Avenova® spray or artificial tears) and follow up provider will be two separate physicians in order to adequately mask the study and prevent any potential bias. All attempts to prevent unmasking of patient treatment arm to the clinician will be attempted.

The patient will return for clinical follow up on days 0,1,2,3,4,5, and week 2 and 3.

On visit day 0,1,2,3,4,5 and week 2 the following will be collected in both groups (Avenova® spray and artificial tears):

Compliance: This study will follow an intention-to-treat analysis. Patient compliance will be assessed each visit and recorded. Non-compliant patients will not be removed from the study as per the intention-to-treat approach. However, the ITT dataset with a per protocol dataset to ensure lack of compliance did not confound the results.

Clinical: Subjective scoring guidelines (see supplemental material) as well as physical exam findings (lymphadenopathy, follicular conjunctivitis, injection, discharge, subepithelial infiltrates, conjunctival pseudomembranes) *See Objective Questionnaire*. Compliance will be assessed each visit and recorded.

Samples: Samples of the tears from the ocular surface and conjunctiva will be obtained through cotton swabs. Collected samples will be sent to the Bascom Palmer Microbiology laboratory for PCR evaluation and microbiology evaluation and then promptly disposed of.

Patients will be questioned about adverse events each visit and be assessed for surrounding periorbital dermatitis.

On visit week 3 (medical only visit):

During the preceding week, the patient has not received any treatment. During this visit, no samples will be taken. This is a medical only visit to ensure proper medical follow up and continued symptomatic relief from the viral conjunctivitis.

8) **Statistical Protocol***

Viral conjunctivitis

POWER ANALYSIS:

%spontaneous resolution in 7 days: 20%

%Resolution with treatment: 50%

(Resolution as defined previously— resolution of follicular conjunctivitis by clinical examination (no follicles on tarsal conjunctiva) and symptomatic improvement in viral conjunctivitis by questionnaire.)

N=39 for each treatment group for power of 80%

Statistical analysis will be performed using Kaplan-Meier survival analysis and Cox proportional hazards regression using SAS version 9.4 (Cary, NC, USA). A p-value ≥ 0.05 will be considered statistically significant.

9) **Provisions to Monitor the Data to Ensure the Safety of Subjects***

Subjects will return for follow up appointments for three weeks total. It is safe to monitor these patients at these intervals as these viral infections are self-limiting and often resolve with time. As there is currently no treatment for these infections, observation and symptomatic management is standard of practice.

Co-investigators on the study will assess patients at each of the follow-up visits for any adverse events during the use of the assigned medical treatment and document this in the electronic medical health record. Patients will be given the telephone number of a principle investigator for use if they believe they are having a significant side effect or may also present at the 24 hour emergency department at the Bascom Palmer Eye Institute. If there are noted adverse reactions during use of the device, participation in the study will be evaluated and if deemed necessary, the patient will be terminated from the study.

10) **Withdrawal of Subjects***

Patients may withdraw voluntarily from the study at any time, but will continue to be followed outside of the study for their viral conjunctivitis.

11) **Risks to Subjects***

Avenova® (0.1% hypochlorous acid) has been extensively studied and has been cleared by the FDA as a 510(k) medical device wound cleanser for any skin and has undergone extensive in-vitro toxicity testing. In ophthalmology, it is commonly used as a lid cleanser in the treatment of blepharitis and meibomian gland dysfunction. It is applied directly to the lid margin and has an excellent safety profile. There have been no noted ocular side effects, including a lack of ocular irritation. (See included “Material safety data sheet”.)

We see no foreseeable risk to the artificial tear group.

There is no foreseeable risk of obtaining the cotton swabs from the conjunctiva. These tests will be performed at no additional cost to the patient.

Exclusion criteria include pregnancy and thus this group would not be included in the study. Those who may become pregnant during the study may choose to leave the study—however the topical spray is safe to be used in pregnancy.

12) **Potential Benefits to Subjects***

Benefits to patients would include earlier resolution and discomfort from conjunctivitis compared to control. These treatments could shorten duration of viral conjunctivitis, a common and extremely contagious viral infection that stops patients from carrying out their normal activities. If our study shows a shortened duration of infection from this therapy, it could result in a new approach for symptomatic relief from the effects of viral conjunctivitis.

13) **Setting**

Bascom Palmer Eye Institute is an ophthalmic hospital with a 24 hour emergency department specializing in ophthalmic disease. Research will be collected as the patient is followed in the emergency department as well as by physicians staffing clinic.

14) **Resources Available**

Bascom Palmer Eye Institute is an ophthalmic hospital with a 24 hour emergency department specializing in ophthalmic disease. The institute receives a wide referral base including all of Florida and the surrounding sites, as well as numerous international referrals due to its prominence in the field of ophthalmology. This institute is staffed with residents, fellows and attending physicians, all specialized in the field of ophthalmology. Each week, the emergency department diagnoses at least 10 cases of viral conjunctivitis.

Before the start of the study, all participating members will be informed of the study, as well as possible risks, benefits and their role within the study.

15) **Recruitment Methods**

Patients will be recruited from the Bascom Palmer Eye institute emergency department as a referral. Potential subjects are those identified as being infected with viral conjunctivitis by the ophthalmologist. There will be no advertisements for this study and no payment will be offered to participants of the study. If the patient consents to the study, he/she will be randomly assigned to Avenova® vs artificial tears through a randomization computer program.

16) **Confidentiality**

Identifiable data will be stored on a locked and encrypted USB drive to be locked in the office of Dr. Lee on the 4th floor Suite 450M of the Bascom Palmer Eye Institute located at 900 NW 17th Street, Miami, FL 33136. This data will be de-identified of personal identifying information at the conclusion of the study. The investigatory team will assign subject identifiers and study records will only be accessed by the study coordinators.

17) **Provisions to Protect the Privacy Interests of Subjects**

To limit intrusiveness to patients, data will only be collected during clinic follow-ups.

18) **Compensation for Research-Related Injury**

Patients will not be compensated for research related injuries. This will be written in the consent and described to the patient before participation in the study.

19) **Economic Burden to Subjects**

The device will be provided free of cost to patients as provided by NovaBay. Also, there is no cost to participants for the collection of tears via the use of cotton swab.

20) **Consent Process**

Consent will be obtained during an Emergency Room visit by the physician and will follow the SOP: Informed Consent Process for Research (HRP-090). The informed consent will occur that same visit to the ER; if the patient decides that he/she does not want to participate, he/she will be unable to participate at a later visit. The patient will have the ability to discontinue to the study at any time.

Non-English Speaking Subjects

- Spanish will be used to obtain consent in those who prefer the Spanish language—translation will be offered if needed with consent offered in the Spanish language.

21) **Process to Document Consent in Writing**

Eligible subjects will be informed of the nature, risks, and benefits of the study and informed that they are not required to participate. If interested in participating, they will be given the consent form to read, asked if they have any questions or need further explanations.

The consent process will be obtained by one of the research team members whose

name and signature will be mentioned in the consent form. The details of the study will be explained to the prospective subjects.

22) **Drugs or Devices**

The device will be stored, handled and dispensed by the Bascom Palmer Pharmacy and the designated IRB study team members. The device will be administered by the patient. Avenova® has received FDA clearance as a 510(k) medical device with a wide range of indications including for use on the skin surface. Artificial tears are commonly used on the ocular surface to lubricate the eyes such as in cases of dry eye syndrome.

References

1. Kim HJ, Lee JG, Kang JW, Cho HJ, Kim HS, Byeon HK, Yoon Effects of a low concentration hypochlorous acid nasal irrigation solution on bacteria, fungi, and virus. *H.Laryngoscope*. 2008 Oct;118(10):1862-7
2. Debabov D, Noorbakhsh C, Wang L, et al. Avenova™ with Neutrox™ (pure 0.01% HOCl) compared with OTC product (0.02% HOCl). NovaBay Pharmaceuticals, Inc., Emeryville, California, USA.