Study Title: Topical bimatoprost for chemical blepharoplasty

1. Study aim, background, and design

Study aim:

Topical bimatoprost has been shown to cause periorbital changes of soft tissue which are most pronounced when used directly onto the cornea for the treatment of glaucoma. Changes are primarily felt to be the result of prostaglandin-mediated adipocyte loss, resulting in deepening of the upper eyelid sulcus and recession of infraorbital pseudoherniation. Use of topical bimatoprost to the upper eyelid margin, now FDA approved for eyelash enhancement, may provide a metered effect on the periocular tissues and allow for a topical approach to periocular rejuvenation. I propose a proof of concept, small scale study to identify change in dermatochalasis with use of bimatoprost along the lid margin.

Background:

Perception of beauty in the periocular region is influenced by several factors, including symmetry, population norms, and skin texture and tone. Soft tissue and skin changes over time create an aged appearance with the development of dermatochalasis, blepharoptosis, lacrimal gland prolapse, and fat prolapse[1]. Techniques for periocular rejuvenation are well established and include soft tissue augmentation, resurfacing, and surgical correction. In May 2015, Sarnoff and Gotkin reported a case of "chemical blepharoplasty" achieved with topical bimatoprost ophthalmic 0.03% solution applied to the upper eyelid margin. After three months of use, the author noted a more youthful appearance of the periocular region, with deepening of the upper eyelid sulcus, reduction in dermatochalasis, and diminution of the inferior eyelid fat pad. These changes were attributed to the prostaglandin associated periorbitopathy (PAP), a well described phenomenon observed with the use of topical prostaglandin analogues use for glaucoma.

Periorbital changes observed with topical prostaglandin analogues are primarily due to effects on aponeurotic and deep orbital adipocytes[3]. Prostaglandins activate the adipocyte MAPK pathway, leading to inactivation of PPAR-gamma, inhibition of adipocyte differentiation, and decreased fat accumulation within adipocytes[1,4]. Bimatoprost concentration-dependent contractions of ciliary muscles and activation of matrix metalloproteinases[3] may also contribute to periocular changes. Patients using topical ophthalmic prostaglandin analogues commonly develop periorbital fat loss, which has been well characterized in the ophthalmology literature.

Bimatoprost applied to the upper eyelid margin for eyelash enhancement attempts to capitalize on the desirable effects of darker, longer, thicker eyelashes, while limiting more significant and undesirable effects through limited exposure of the drug to ocular tissues. This same concept

may apply for dermatochalasis: at a metered dose, topical bimatoprost to the lid margin could lead to subtle periorbital fat loss resulting in improved dermatochalasis.

Study design:

This is a proof of concept study which aims to enroll a series of patients with mild to severe dermatochalasis, treat with topical bimatoprost 0.03% solution to the upper lid margin, and evaluate for cosmetic improvement of the periocular area.

15 subjects will be recruited.

2. Subject Population

Inclusion criteria: 18+, mild to severe dermatochalasis, desire for enhanced eyelashes

Exclusion Criteria: Patients with current use of ophthalmic prostaglandin analogues, history of blepharoplasty, history of neuromodulators or fillers to the periocular region or frontalis in the last 6 months, existing deep upper eyelid sulcus, opposition to eyelash enhancement, pregnancy *(This small proof of concept series aims to look at a new use of an already FDA approved medication. Currently this medication is pregnancy category C and has not been studied in children. As such we will only expose the patient population in which this medication has been determined to be safe.)*

Patients will be recruited through our medical dermatology and cosmetic dermatology clinics at our University by faculty and residents based on inclusion criteria.

Recruiting script:
"I am doing a study looking at the use of the medication Latisse, which is currently FDA approved for eyelash enhancement, for possible effects it could have on drooping eyelids, or dermatochalasis. Involvement in the study would involve use of the product nightly as well as monthly visits for 4 months. Would you be interested in getting more information on this study?"

3. Procedure

At the initial visit, the study as well as known benefits and side effects of topical bimatoprost will be discussed with the patient. Written informed consent will be obtained for study inclusion, treatment, and photographic documentation. An initial examination and photodocumentation will be performed, and application instructions per the package insert. ("…should be applied every night using only the accompanying sterile applicators. They should start by ensuring their face is clean, all makeup is removed, and their contact lenses removed (if applicable). Then, carefully place one drop of LATISSE® solution on the disposable sterile applicator and brush cautiously along the skin of the upper eyelid margin at the base of the eyelashes. If any

LATISSE® solution gets into the eye proper, it will not cause harm. The eye should not be rinsed.")

Potential side effects to be discussed include potential for itching sensation of the eyes or eyelids, intraocular pressure effects, eyelid skin redness or darkening, iris darkening, unexpected hair growth or eyelash changes. Patients will be informed to contact the primary study investigator with any acute ocular changes (trauma, infection), sudden decrease in visual acuity, or eyelid/eye irritation.

The patients will be asked to use the medication nightly, and will be followed with Q 4 weeks appointments for a total of 4 visits.

Data collection:

Demographic information will be collected on all patients, including: age, sex, ethnic background.

An entry survey will be completed requesting self evaluation of the periocular area. **(Appendix A)**

Patients will be followed Q 4 weeks in clinic with followup photodocumentation at each visit for a total of 4 visits, 3 months of treatment.

During each visit, application instructions will be reviewed to ensure appropriate use. Each patient will be asked to complete a survey inquiring about potential side effects to ensure continued safety at followup visits **(Appendix B)**, as well as an exit survey **(Appendix C)**

At completion of the study period, each patient's photographs at weeks 0, 4, 8, and 12 will be graded by 2 blinded evaluators for level of dermatochalasis: -1 (deep upper eyelid sulcus), 0 (no dermatochalasis), 1 (mild, slightly noticeable), 2 (moderate, noticeable), or 3 (severe, distinctive). Grading will be assisted by a visual aid adapted from a scale published by Shah et al. **(Appendix D)**

4. Risks

The patients participating in the study are subject to minimal risk with use of the topical medication. If experienced, side effects such as eye or eyelid irritation, eyelid discoloration, and iris dyspigmentation will resolve with medication discontinuation. Patients may be referred to an appropriate physician specialist if needed. No direct psychological or social harm is expected.

Confidentiality of data will be maintained via a system of de-identification and password protection. First, each patient will be assigned a code (P1-15) by which they will be identified. The code key will be stored in a password protected excel document on the PI's computer. Demographic data as well as survey answers will be stored without patient names (only P#),

again in a password protected excel document.

At the cessation of the study the key will be destroyed, leaving only de-identified information.

Photographs will be taken on a digital memory card reserved only for use in the study. Photographs that include our study area, the eyes, are difficult to de-identify. Photos will include only the eyebrows and eyes in an effort to minimize face recognition. Patients will be asked to sign a separate photograph consent detailing this information.

All data is stored on a password protected laptop to which only the PI has access.

Combined, de-identified data and photographs will be used for medical education, presentations, and publication. This information is included in the consent forms.

5. Benefits

The medication is currently FDA approved for eyelash enhancement. patients can expect to see increased length and density of eyelashes.
Improvement in dermatochalasis may be seen.

6. Remuneration

There will be no payment for participation in this research study.

7. Academic or Extra Credit

NA

8. Costs

There will be no costs to the subject for participating in this research study.

9. Alternatives

The subjects do not have to participate in the research.

10. Consent process and documentation

Written informed consent will be obtained for study participation as well as medical photography.

11. Qualifications of the investigators

The researcher is a physician completing her residency in dermatology in June 2017. She participates in direct patient care and informed consent regularly. She developed the concept and design of this study and is able to properly select appropriate patients, consent them, and provide instruction on appropriate use. Though she has not served as PI for a project

previously, her organization skills have allowed her to give multiple presentations at local, regional, and national conferences and write a dermatology textbook chapter. She is committed to the completion of this project before her graduation in June 2017.

12. References

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