

Title: Silicone Gel for Postsurgical Scars of the Eyelid

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Efficacy of silicone gel versus placebo for postsurgical scars of the eyelids

Study Protocol for Efficacy of silicone gel versus placebo for postsurgical scars of the eyelids

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Principal Investigator, Research Team, and Study Site:

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Research Synopsis:

Study Title: Efficacy of silicone gel versus placebo for postsurgical scars of the eyelids

Study Population: The population includes those with upper eyelid ptosis or dermatochalasis, undergoing surgical treatment. This becomes more common with increasing age. There is a wide range of gender and health statuses included in the study.

Study Design: This is a prospective, double-blinded, split-face randomized study.

Sample Size: 100 patients

Study Duration: 3 years to recruit patients, perform surgeries, collect and analyze data.

Primary Objective: To determine whether silicone gel is effective at preventing or minimizing scar formation after eyelid surgery.

Outcome measures: The outcome measure is scoring of the scar in terms of pigmentation, irregularity, and scar height. Scores will be calculated by a blinded surgeon and by a blinded third-party grader of external photographs taken at routine monthly post-operative visits.

Secondary Objectives: To determine whether silicone gel treatment has any effect on patient satisfaction with post-surgical eyelid scars.

Outcome measures: Pain, itching, and overall satisfaction with the healing process will be rated by patients during postoperative visits.

Background and Significance:

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Upper eyelid blepharoplasty or ptosis repair is performed when the upper eyelid becomes droopy, which often occurs as a natural part of the aging process. The droopiness of the upper eyelids decreases the ability to see objects in their peripheral vision, causing functional deficits. Additionally, the droopiness can be a cosmetic concern for many. The most effective treatment option is blepharoplasty or ptosis repair.

During routine pre-operative counseling, many patients note a fear of prominent facial scarring. Different techniques have been described in the literature to minimize scarring, from steroid creams to injections to laser therapy [1]; however, there is currently no consensus for long-term management of post-surgical eyelid scars. Specifically, there is no study examining the efficacy of topical silicone gel on eyelid scars, although a few studies have examined its efficacy on other facial scars [2-3]. Silicone is proposed to aid in healing by regulating fibroblast production, reducing collagen production, and modifying expression of growth factors [4].

Our study is designed to determine whether topical silicone may prevent significant post-operative eyelid scar formation. It may help clarify whether there is a safe and effective topical treatment for patients undergoing eyelid surgery for whom scarring or cosmesis is a concern. It is the first study of silicone gel on the eyelid and is also prospective, randomized, and double blinded.

Objectives:

Primary Objective: To determine whether silicone gel is effective at preventing or minimizing scar formation after eyelid surgery.

Null Hypothesis: Silicone gel has no effect on improving the cosmetic appearance of post-surgical eyelid scars.

Outcome measures: The outcome measure is scoring of the scar in terms of pigmentation, irregularity, and scar height. Scores will be calculated by a blinded surgeon and by a blinded third-party grader from external photographs taken of patients at routine post-operative visits.

Secondary Objective: To determine whether silicone gel treatment has any effect on patient satisfaction with post-surgical eyelid scars.

Null hypothesis: Silicone gel has no effect on patient satisfaction compared to placebo.

Outcome measures: Pain, itching, and overall satisfaction with the healing process will be rated by patients during postoperative visits.

Study design/methodology:

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In this prospective, double-blinded split-face randomized study, patients who have already consented to undergoing surgical repair of upper eyelid ptosis or blepharoplasty will be asked by the surgeon/principal investigator if they wish to participate in the study. The informed consent process will take place in the PI's office after routine pre-operative counseling and discussion is performed for repair of upper eyelid ptosis or blepharoplasty.

Patients who have consented to the study will receive two tubes labeled only "left" and "right", corresponding to the side of the face to which the tube contents will be applied. One tube will contain silicone gel and the other tube will contain aquaphor. Neither the patient nor the surgeon will know what side will receive which treatment. These tubes will be given to patients at post-operative week 1 visit (prior to this, all patients will receive a combination steroid and antibiotic ophthalmic ointment (like neomycin/polymyxin/dexamethasone (Maxitrol)) to apply to the healing incision site, which is the current standard practice for the surgeon). Patients will be instructed to rub the solution into their eyelid incisions gently with their fingers for 2-3 minutes twice a day.

At post-operative visits monthly until month 6, the surgeon will grade the scars and color pictures of the scars will be taken. These pictures will then be shown to a blinded, objective grader to grade the scars based on vascularity and color. In addition, at each post-operative visit, patients will be provided with a survey rating their satisfaction with scar appearance, as well as information on subjective symptoms like itching or pain. These are measurements that are already collected as standard of care in all such patients, whether or not they are part of this study.

A data safety monitoring board will be established, consisting of an independent ophthalmologist not associated with the study (Dr. Jamie Rosenberg) and a biostatistician (Dr. Moonseong Heo). The DSMB will meet once at the halfway mark and perform an interim analysis.

We will conduct an interim analysis in the middle of the trial when the half of the total number of subjects are evaluated. If the interim analysis resulted in a two-sided p-value < 0.001 (Peto boundary), then we will stop and discontinue the trial, and declare a superiority of an intervention which shows a greater effect

*Scoring Questionnaire:***FOR THE BLINDED GRADER - RIGHT/LEFT****ERYTHEMA**

- 1 = none
- 2 = pink
- 3 = red

ELEVATION

- 1 = no elevation
- 2 = minimal elevation $< 0.5\text{mm}$
- 3 = definite elevation $> 0.5\text{mm}$

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PIGMENTATION

1 = normal

2 = hyper- or hypo-pigmentation

FOR THE PATIENT – RIGHT/LEFT:

How satisfied are you?

1 = very dissatisfied

2 = dissatisfied

3 = neutral

4 = satisfied

5 = very satisfied

Do you have significant itching of your surgical site?

1 = None

2 = Occasional

3 = Requires medication

Are you experiencing pain?

1 = None

2 = Occasional

3 = Requires medication

How smooth do you think your scar is?

1 = Normal

2 = Soft/Supple

3 = Hard

Which eyelid has the more pleasing appearance to you? Right or left?

Study Population:

The population includes those with upper eyelid ptosis requiring surgical treatment, which most commonly affects patients greater than 50 years. There is a wide range of gender and health statuses.

Inclusion /Exclusion Criteria:

Patients will be included if they have met the criteria for undergoing upper eyelid ptosis repair or blepharoplasty. This means they have droopiness of the upper eyelids that is visually significant and limiting the patient's visual field.

Patients will be excluded if younger than 18 years old, or if they require additional upper eyelid surgery.

Study Duration/ Study Timeline:

Stage 1, recruitment and performance of surgeries ----24-30 months

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Stage 2, data collection and data analysis----1-2 months

Stage 3, presentation and publication----1-2 months

Projected start date: May 1, 2018

Total length of time: 3 years

Approximate end date of the study: May 1, 2021.

Statistical Analysis Plan:

The data will be analyzed to determine whether there is any difference between scar pigmentation or irregularity between the two sides. This will be done at each of the time points, post-operative week 1, post-operative month 1, post-operative month 3, and post-operative month 6. The primary outcome data will be the post-operative month 6 data on scar erythema, elevation, pigmentation; secondary outcome data will be the post-operative month 6 data on pain, itching, and patient preference between the two eyes. For this to be accomplished with sufficient power, biostatistician, Dr Moonseong Heo, has calculated that we will need approximately 100 patients, also taking into account for patient attrition and/or missing data.

We also plan to perform an interim analysis at month 3 for efficacy.

To test the effect of the treatment we will apply mixed effects linear model with AR(1) covariance structure to account for the within-subject monthly outcome correlations over the six-month study period.

Power analysis:

The table below displays the number of subjects required to detect 0.3 SD unit difference in outcome means between placebo and the active treatment with 80% power at a two-sided significance level of 0.05 under the following RCT design parameters: 1) the active treatment will be randomly assigned to either eye and the other eye will be treated with a placebo; 2) participants will be followed up every month for six months after baseline; 3) the outcome correlation between eyes within subjects are denoted by rho_2; and 4) the outcome correlations across 6 follow-up months within subjects are denoted by rho_1.

	Rho 1		
Rho 2	0.4	0.5	0.6
0.05	79	94	108
0.1	70	85	99
0.2	53	67	82

In conclusion, with the planned recruitment of 75~100 subjects, our study is adequately powered to detect >0.3 SD unit difference in outcome means between placebo and treatment eyes.

Informed Consent Process:

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For this prospective data collection, we will use a consent form to obtain informed consent in order to include the patient in the study. The language and writing of an informed consent is at a 6th grade level. For those not speaking English, a HIPAA compliant language services provider will be used and the name of the interpreter, along with their interpreter number documented. We will not be targeting potentially vulnerable subjects to be enrolled in the study, such as pregnant and lactating women, children, prisoners, cognitively impaired and critically ill subjects.

Privacy and confidentiality:

Human subject's names will be kept on a password protected database and will be linked only with a study identification number for this research. There are no patient identifiers. External photographs will be limited to upper eyelid tissue and photos will not show any identifying features. All data will be entered into a computer that is password protected. Data will be stored in a locked office of the investigators and maintained for a minimum of three years after the completion of the study.

Risk/Benefit:

The risks include those related to the actual surgery, which patients would be undergoing, even if they choose not to be part of the study. These surgical risks include but are not limited to bleeding, scarring, infection, overcorrection, undercorrection, need for reoperation, loss of vision, loss of eye. An additional risk that the study poses is sub-optimal healing of an incision and/or scarring.

This study does not present any direct benefit to the participants. However, the study does provide an opportunity to gain a better understanding of long-term scar management. This will allow us to better counsel patients on post-surgical care after upper eyelid surgery.

Data Safety Monitoring:

The data safety monitoring will be under ongoing review throughout the study's duration. Any action resulting in a temporary or permanent suspension of the study will be reported to the IRB and to the Office of Clinical Research. The PI will be responsible for reporting any reasons outside the planned study design such as non-compliance with the protocol or if there is any delay in the initiation of the study due to administrative reasons. If interim analysis of data reveals a clear inferiority in one of the procedure outcomes, the study will be stopped. Specific conditions for immediate suspension of the study include the following: 1) if postoperative outcomes, as measured by patient surveys, are consistently rated poor.

Conflict of Interest:

PI has no consultative relationships that could be considered an apparent conflict of interest.

Publication and Presentation Plans:

The plan is to present the data and results of this study as an article submission to the journal, Plastic and Reconstructive Surgery.

References:

1. Murdock J, Sayed MS, Tavakoli M, et al. Safety and efficacy of a growth factor and cytokine-containing topical product in wound healing and incision scar management after upper eyelid blepharoplasty: a prospective split-face study. Clin Ophthalmol 2016;10:1223-8.
2. Bianchi FA, Rocchia F, Fiorini P, Berrone S. Use of patient and observer scar assessment scale for evaluation of facial scars treated with self-drying silicone gel. J Craniofac Surg 2010;21(3):719-23.
3. Yun IS, Yoo HS, Kim YO, Rah DK. Improved scar appearance with combined use of silicone gel and vitamin C for Asian patients: a comparative case series. Aesthetic Plast Surg 2013;37(6):1176-81.
4. Puri N, Talwar A. The efficacy of silicone gel for the treatment of hypertrophic scars and keloids. J Cutan Aesthet Surg 2009;2(2):104-106.