Wayne State University

Topical 5% Tranexamic Acid as a Treatment for Post-inflammatory Hyperpigmentation due to Acne Vulgaris

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1.0 Background

Post-inflammatory hyperpigmentation (PIH) is a common occurrence following skin inflammation, whether due to trauma or inflammatory dermatoses, often leading to long-term dyschromia which may last years after the inciting lesion has resolved. PIH is an acquired hyperpigmentation caused by hypermelanosis after cutaneous trauma or inflammation, and while it may occur in any skin type, is more commonly found in darker skin (Fitzpatrick skin types IV-VI)[1]. These discolorations often occur on cosmetically sensitive areas, such as the face, and may lead to tremendous psychological impact.[2] Tranexamic acid (TA) is a plasmin inhibitor capable of inhibiting melanogenesis, and has been previously taken orally, injected intradermally, and more recently applied topically for treatment of melasma.

2.0 Rationale and Specific Aim

The goal of this study is to determine if topical 5% TA is capable of reducing the severity of PIH following acne vulgaris. Topical hydroquinone represents the current standard of care for PIH, however, common side effects include irritation, erythema, and dermatitis—side effects not reported in topical TA.

3.0 Previous Studies

Several studies have demonstrated topical TA provides statistically significant improvements in women with melasma, another cause of hyperpigmentation. Additionally, it has been demonstrated to be equally effective as hydroquinone in reducing melasma hyperpigmentation, however with less adverse effects[2].

4.0 Inclusion/Exclusion Criteria

Inclusion Criteria:

- Age 18-65
- Patients with bilateral involvement of facial PIH secondary to acne vulgaris.

Exclusion Criteria

- Pregnant patients or patients planning to become pregnant during the time of the study.
- Patients with a history of use of hydroquinone, kojic acid, tretinoin, adapalene, tazarotene or azaleic acid in the previous 3 months

5.0 Enrollment/Randomization

Patients presenting to the dermatology clinic with PIH secondary to acne vulgaris and are interested in a potential treatment will be considered as candidates for participation. If their treating physician in clinic determines they are eligible, they will be referred to the PI or sub-PI for screening and consent. The study design and consent will be explained, their expectations for participation will be discussed, and any questions will be addressed. The patient will then have the choice to participate or decline participation in the study. Block randomization will be utilized to determine which side will be the treatment side.

6.0 Study Procedures

Patients with bilateral disease will be chosen to participate in the study. Patients will be advised to discontinue any other facial cleansers or products prior to beginning treatment. One side of the patient will be chosen as the treatment side, and the other as an intrinsic control. Each day, the participant will wash their face in the morning with a standard cleanser, dry their face, then apply the medication to the treatment side of their face only to areas of unwanted dark spots. The patient will then apply the vehicle to the other side of their face only to the areas of unwanted dark spots. The patient will wait 30 minutes, and then apply a standardized sunscreen SPF 30+ to entire face. Each night, the patient will again wash their face with the standard cleanser, and apply the two medications to the proper side of their face. Patients will participate in a follow-up clinic visit 4 weeks, 8 weeks and 12 weeks after beginning treatment. At each visit, photographs will be taken of their face to monitor progression and to serve as a comparison to the control side. The postacne hyperpigmentation index, a validated system for evaluating hyperpigmentation due to acne vulgaris, will be used to monitor the progression of facial lesions.[7] At week 0 and 12, the patients will take a survey to determine the impact that their facial spots have on their quality of life.

7.0 Risks

Risks of topical TA include skin erythema and irritation. There may also be risks involved with this with this study that are unknown to the researcher at this time.

8.0 Study Withdrawal/Discontinuation

The participant is free to withdraw from the study at any time. He/she should inform the primary investigator or any co-investigator.

9.0 Statistical Considerations

We will attempt to demonstrate clinical improvement of the postinflammatory hyperpigmentation by decreasing the size, intensity, and number of the facial lesions by comparing the treatment side to the control side of the face.

Patients will be evaluated prior to treatment, and at each follow-up visit both 4 weeks, 8 weeks and 12 weeks post-treatment using the Postacne Hyperpigmentation Index (PAHPI). The scoring system is as follows:

Table I. Scoring the postacne hyperpigmentation index

Weighted score (S)	Median lesion size
2	<3 mm
4	3-6 mm
6	7-10 mm
8	>10 mm

Weighted score (I)	Median lesion intensity
3	Slightly darker than surrounding skin
6	Moderately darker than surrounding skin
9	Significantly darker than surrounding skin

Weighted score (N)	No. of lesions
1	1-15
2	16-30
3	31-45
4	46-60
5	>60

Total postacne hyperpigmentation index = S + I + N; score range: 6-22.

Using power analysis to determine sample size:
In the study by Kim et al,[4] they demonstrated a significant decrease in melasma, another disorder of facial hyperpigmentation, using topical tranexamic acid. They demonstrated a significant decrease in the melasma area and severity index of approximately 33% with a sample size of 23 patients. For our study, a sample size of 25 patients is sufficient to detect a clinically important difference of 30% between treatment and control sides of the face using a two-tailed z-test of proportions between two groups of 80% power and a p-value of 0.05.

10.0 Privacy/Confidentiality Issue

Data will be tabulated on a password-protected excel sheet stored on the principal investigator's computer. This computer will be stored in the WSUPG Department of Dermatology. All patients will be de-identified and labeled using a coding system (001, 002, etc).

Patients will have photographs taken of lesions at each visit. Photographs may be used in publications or presentations. Full-face photographs will be taken, an attempt will be made to de-identify the photograph as much as possible, including a black box over any distinguishing features.

11.0 Follow-up and Record Retention

Each participant will be enrolled in the study for 12 weeks with a total of 3 clinic visits. During these 12 weeks, the clinic visits include: 1 visit for initial baseline evaluation, and three follow-up appointments at 4 weeks, 8 weeks and 12 weeks of treatment. All pictures will be stored

securely on the dermatology department password protected hard drive and all data will be deleted at the end of the study.

12.0 References

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