BRIEF ARTICLES

Expedited Resolution of 5-Fluorouracil-Induced Reaction and Barrier Dysfunction with White Petrolatum

Melody Maarouf MHS[1], Bryan W. Kromenacker MA BSN[1], Eric E. Brucks MD[2], Vivian Y. Shi MD[3]

[1]University of Arizona, College of Medicine, Tucson, AZ
[2]University of Arizona, Department of Medicine, Tucson, AZ
[3]University of Arizona, Department of Medicine, Division of Dermatology, Tucson, AZ

ABSTRACT

Actinic keratoses (AK) are precancerous lesions that develop on chronically sun-exposed skin. They frequently require prophylactic field treatment due to the risk of progression to squamous cell carcinoma. Topical 5-fluorouracil (5-FU) is highly effective treatment for AK, yet leaves a patient with an exuberant erythematous reaction at treatment site, which can be embarrassing and uncomfortable. We report a case of a patient with diffuse facial AK who was treated with 5-FU twice daily for 2 weeks, resulting in fiery-red erythema and disrupted barrier function. Application of pure ultra white petroleum jelly, an emollient preferred by dermatologists for post-operative wound healing, resulted in drastic decreased erythema and recovery time of post-treatment transepidermal water loss and hydration, compared to the contralateral, non-petrolatum-treated side. Additionally, petrolatum use did not disrupt the AK resolution endpoint. We suggest that petroleum jelly be used for the repair of 5-FU-induced barrier disruption and erythema to promote greater patient adherence.

INTRODUCTION

Topical 5-fluorouracil (5-FU) is a commonly prescribed field treatment for diffuse actinic keratosis (AK).[1] 5-FU preferentially targets AKs, inducing inflammation and skin barrier disruption, [2] with erythema, blistering, necrosis with erosion, and re-epithelialization. Complete AK clearance can be seen in up to 90% of patients who tolerate these side effects. [3]

There is no standard recommendation on post-topical 5-FU wound care to minimize skin discomfort and inflammation. Previously, Erlendsson et al. attempted to mitigate the cutaneous reactions associated with topical ingenol-mebutate. Following finalization of AK treatment, twice-daily application of topical Clobetasol proprionate 0.05% for 4 days did not show significant reduction of local skin responses, pain, or pruritus. [4] Maarouf et al., have shown that petrolatum is effective in improving post 5-FU erythema and skin hydration. [5]

CASE REPORT

A 67-year-old Caucasian male with diffuse facial AK (19 by count; left: 10 right: 9)

underwent 5-FU treatment twice daily for 2 weeks. Within 1 week, he experienced erythema, burning, and itching, which became robust and uncomfortable during the second week of treatment. After completing his 5-FU course, he applied Vaseline Pure Ultra White Petroleum Jelly (Covidien, Mansfield, MA) to the right side of the face twice daily for 2 weeks, leaving the left side of the face untreated.

Four weeks following 5-FU initiation, 95% AK lesions had resolved and no lesion was present at 3 months follow-up. Average Clinician's Erythema Assessment (0=clear skin with no signs of erythema to 4=severe erythema/fiery redness)[6] and skin barrier biophysical properties [hydration, transepidermal water loss (TEWL)] were measured at baseline, weekly during 5-FU treatment, and for 2 more weeks during petrolatum intervention.

Facial erythema, hydration, and TEWL progressively worsened during 5-FU treatment, peaking at 3-weeks. Compared to the contralateral control side, petrolatum significantly reduced erythema, increased hydration, and decreased TEWL (Figure 1A-D).

Hydration steadily declined throughout treatment, and sharply rose by week 5. In mixed-effects bivariate regressions across ointment conditions using face side as the grouping variable, erythema positively correlated with TEWL ($r = 0.42$, $p = 0.03$) (Figure 1E) and inversely correlated with hydration ($r = -0.57$, $p = 0.004$) (Figure 1F), suggesting that subjective erythema accurately reflected changes in skin barrier physiology.

DISCUSSION

While an important therapy for prevention of SCC, topical 5-FU is uncomfortable (Figure 1A-C). The inflammatory response severity correlates closely with the degree of barrier dysfunction that persists weeks after the initiation and cessation of 5-FU use (Figure 1D-E). Thus, facial treatment is especially intolerable and cosmetically unacceptable. This report demonstrates that white petrolatum, a bland, cheap, and widely available barrier repair ointment, can significantly reduce erythema and repair barrier dysfunction.

Petrolatum is a semisolid mixture of hydrocarbons derived from heavy mineral oils, which resemble the components of intercellular epidermal lipids. In addition to forming a hydrophobic film on the skin surface, petrolatum's hydrophobic nature allows it to diffuse into the epidermis. Intercalation into intercellular spaces promotes modification of the lipid lattices to reinforce barrier integrity. [7]

The therapeutic advantage of 5-FU is in disaccord with its high rates of symptomatology dissatisfaction. The prospect of lessening adverse effects and time to erythema resolution may increase patient tolerance and compliance for 5-FU treatment. Additionally, the 100% resolution of AK count suggests that petrolatum does not reduce 5-FU efficacy.

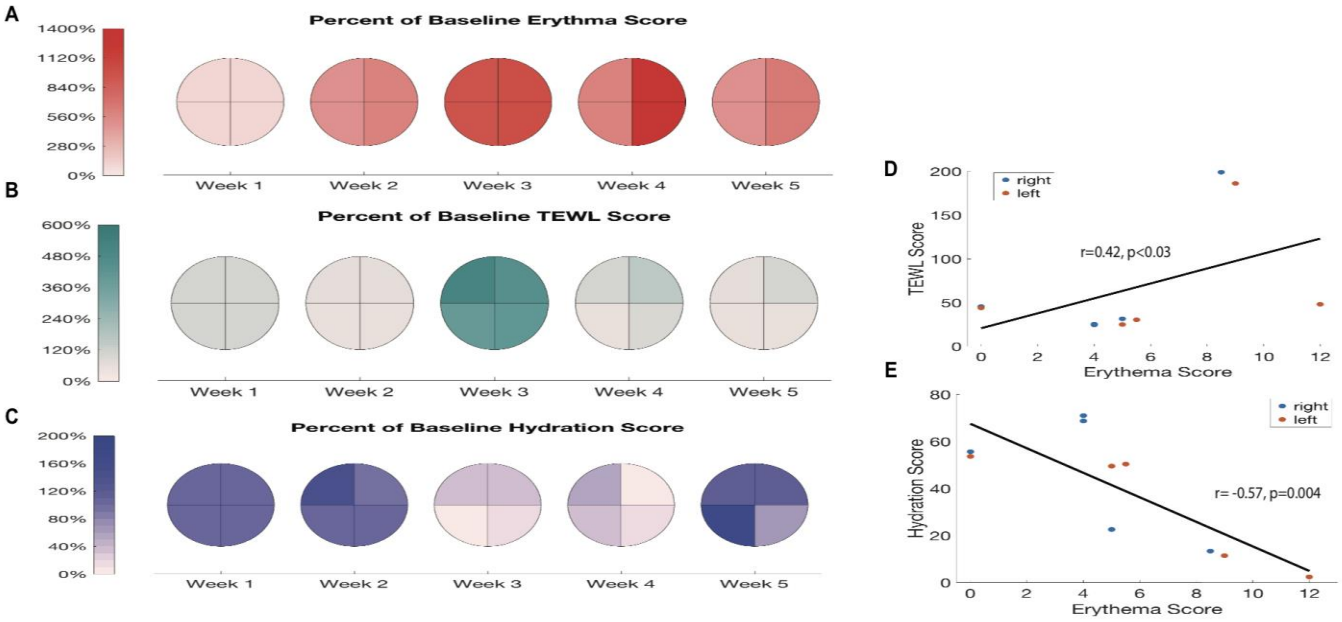

Figure 1. (a) Heatmap represents progressively increasing erythema during5-FU treatment (Weeks 1-3), with decreasing erythema on the petrolatum-treated (R) side as early as Week 4; Heatmap represents progressively worsening skin barrier function, characterized by (b) increased TEWL and (c) decreased hydration during 5-FU treatment (Weeks 1-3), with faster recovery detected on the petrolatum-treated (R) side as early as Week 4, compared to the non-petrolatum-treated (L) side; (d) Scatterplot represents a positive correlation (r=0.42, p=0.03) between erythema and TEWL; (e) Scatterplot represents a negative correlation (r=-0.57, p = 0.004) between erythema and hydration.

CONCLUSION

White petrolatum is an effective therapeutic agent in reducing erythema and expediting skin barrier recovery following topical 5-FU. Randomized controlled studies should aim to assess the erythema- and pain-reducing effects that alternative barrier repair modalities have on 5-FU-treated skin

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Corresponding Author:
Vivian Y. Shi, MD
Assistant Professor of Medicine, Dermatology Division
University of Arizona
vshi@email.arizona.edu

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