The Use of a Cream Containing 4% Hydroquinone, 10% Buffered Glycolic Acid, Vitamin C, Vitamin E, and Sunscreen in the Treatment of Postinflammatory Hyperpigmentation in Skin Types IV-VI

Fran E Cook-Bolden, MD[1]

[1]The Ethnic Skin Specialty Group, New York, NY, USA; [1]Columbia University Department of Dermatology, New York, NY, USA

ABSTRACT

Introduction: Postinflammatory Hyperpigmentation (PIH) is a common disorder and can be a major concern, especially in patients with darker skin types.

Objectives: To assess the safety and efficacy of a cream containing 4% hydroquinone, 10% buffered glycolic acid, vitamin C, vitamin E, and sunscreen (Glyquin®, ICN Pharmaceuticals) in depigmenting PIH on the face and body.

Methods: A total of 35 patients with skin types IV, V, and VI and PIH underwent twice daily application with the study cream for 12 weeks. Changes in pigmentation were assessed at monthly intervals, both clinically and with mexameter readings of melanin content and erythema. Patient and physician Global Severity Assessments were also made at each monthly visit.

Results: Mexameter results documented an improvement in PIH using the study cream at as early as 4 weeks in 79% of patients and in 100% of patients at 12 weeks. Both patient and physician global assessment showed an improvement in most patients at 4 weeks. Eighty-nine percent of patients reported no significant symptoms. No serious adverse events occurred during therapy.

Conclusions: A cream containing 4% hydroquinone, 10% buffered glycolic acid, vitamin C, vitamin E, and sunscreen demonstrated good to excellent efficacy and tolerability after 12 weeks of therapy for postinflammatory hyperpigmentation in skin types IV-VI.

INTRODUCTION

Postinflammatory Hyperpigmentation (PIH) is defined as an area of skin discoloration (darker than the normal unaffected skin) at the site of a previous inflammatory process. PIH may develop secondarily to acne, eczema, trauma (eg, laser resurfacing of the skin[1,2]), or irritation (eg, secondary to temporary tattooing with henna[3]). Clinically it presents as brown to black macules and patches, which assume the shape, size, and distribution of the preceding dermatosis.[4] The intensity of the hyperpigmentation may be related to both the nature of the preceding dermatosis and the degree of prior inflammation.

PIH may appear on the face, trunk, or extremities. The disorder can be a major concern for patients with Fitzpatrick skin types IV, V, and VI, in whom it is most prevalent.

Treatment of PIH involves the use of broad-spectrum sunscreens, pharmacological agents, and/or superficial peeling agents.

A cream containing 4% hydroquinone, 10% buffered glycolic acid, vitamin C, vitamin E, and sunscreen (Glyquin®, ICN Pharmaceuticals) has previously been shown to be successful in depigmenting epidermal melasma of the face.[5] Hydroquinone functions to inhibit the enzyme tyrosinase, thereby slowing the conversion of L-dopa to melanin. It is believed that glycolic acid may reduce the thickness of the stratum corneum,[6] thereby enhancing the penetration of hydroquinone. Ascorbyl palmitate (vitamin C) and tocopherol acetate (vitamin E) reduce erythema that is induced by UV exposure.[7] In addition, the study preparation is notable in that it does not expose the patient to sodium metabisulfite, a preservative that is a known to be an allergen to those sensitive to it,[8] particularly patients with asthma.[9] This study was performed to assess the safety and efficacy of this combination of ingredients in depigmenting postinflammatory hyperpigmentation on the face and body in Fitzpatrick skin types IV-VI.

METHODS

Key Inclusion Criteria:

- Fitzpatrick skin types IV-VI
- Clinical diagnosis of postinflammatory hyperpigmentation (PIH) of the face or body

Key Exclusion Criteria

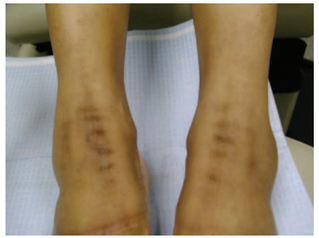
- Exposure in the last 2 weeks to:
  - Topical corticosteroid, bleaching product, azelaic acid, alpha-hydroxy or beta-hydroxy acid, or retinoid
  - UV light therapy or sunbathing
- Treatment with the following oral medications: systemic corticosteroids within 30 days, systemic retinoids within 120 days, other systemic photosensitizing drugs within 120 days
- Known sensitivity to Glyquin® or any of its ingredients
- Patients who have melasma or who are immunocompromised

Study Design

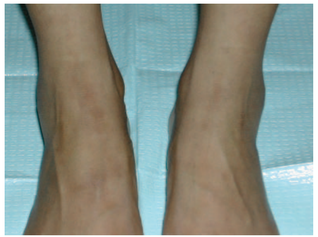
- 4-week washout period followed by baseline evaluation including initial examination and diagnosis of postinflammatory hyperpigmentation
- Visit schedule: baseline, 4 weeks, 8 weeks, and 12 weeks
- Treatment regimen:
  - A cream containing 4% hydroquinone, 10% buffered glycolic acid, vitamin C, vitamin E, and sunscreen (Glyquin®, ICN Pharmaceuticals) (study cream) was applied to the target area BID
  - Patients were instructed to avoid the sun and to restrict their skin-care routine to a cleanser twice daily (Free & Clear® Liquid Cleanser, Pharmaceutical Specialties), a moisturizer (Gly Derm® Hydrotone Lite, ICN Pharmaceuticals) as needed, and a daily sunblock (Gly Derm® Super Sunblock SPF 25, ICN Pharmaceuticals)
- Photographs taken under standard conditions at baseline and at weeks 4, 8, and 12
- Mexameter measurement (mean of 3 readings) of pigmentation and erythema were performed on both the target lesion and normal skin
- Patient and Physician Global Severity Assessments were performed utilizing a four-point visual scale (1=none, 2=mild, 3=moderate, 4=severe)
- Clinical grading of irritation was performed at each visit for both objective (erythema, scaling/peeling, edema, crusting, erosions) and subjective (burning, itching, pain, overall irritation) measures on a five-point scale (0=none, 1=minimal, 2=mild, 3=moderate, 4=severe)
- Improvement from baseline was also rated by both patient and physician on a 5-point scale at each follow-up visit (resolved, significant improvement, slight improvement, no change, or worsening)
- Adverse events were assessed at all visits

RESULTS

Pigmentation Severity

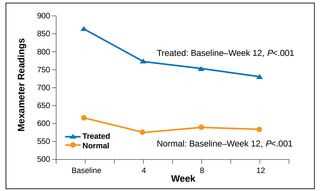


Baseline



12 Weeks

Mexameter Averages

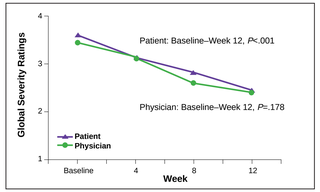


- Based on mexameter readings, after 12 weeks of treatment with the study cream, 100% of patients demonstrated improvement in pigmentation in the target areas ($P<.001$) but not in the nontreated areas. ($P=0.178$).
- The mean mexameter reading decreased by 165.3 points in the treated area vs 25.8 points in the nontreated area.

Demographics and Baseline Characteristics

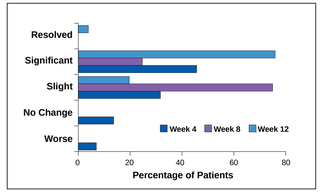
Number of Participants	35
Age range (years)	23-62
Sex	
Male	1
Female	34
Skin types	IV-VI
Postinflammatory Hyperpigmentation Etiology	
Acne	21 (60%)
Irritation	6 (17%)
Trauma	2 (6%)
Other dermatoses	6 (17%)
Minimally or Nonresponsive to prior hydroquinone therapy	24 (69%)

Physician and Patient Global Severity Assessment



- The Patient Global Severity Assessment (on 4-point visual scale) improved significantly, from a mean of 3.6 points at baseline to a mean of 2.4 points after 12 weeks ($P<.001$).
  - Patient Global Severity Assessments improved by 2 points in 8/25 patients (32%) and by 1 point in 11/25 patients (44%).
- Similarly, the Physician Global Severity Assessment fell from a mean of 3.4 points at baseline to a mean of 2.4 points ($P<.001$).
  - Physician Global Severity Assessments improved by 2 points in 6/25 patients (24%) and by 1 point in 14/25 patients (56%).

Percentage of Patients With Improvement (Physician Assessment)



- After 12 weeks of treatment, 80% of patients demonstrated significant improvement or resolution of their PIH lesions relative to baseline, based on physician assessment.

	Week 4					Week 8					Week 12				
Patient Evaluation:	Minimal	Mild	Moderate	Severe	Total	Minimal	Mild	Moderate	Severe	Total	Minimal	Mild	Moderate	Severe	Total
Burning	2	1	2	1	6/32 (19%)	3				3/25 (12%)	1	1			2/25 (8%)
Itching	1	1	1		3/32 (9%)	2				2/25 (8%)					0/25 (0%)
Irritation	3	1		1	5/32 (16%)	3				3/25 (12%)	2				2/25 (8%)

DISCUSSION

- Postinflammatory hyperpigmentation (PIH) is a major concern, especially among patients with Fitzpatrick skin types IV-VI.
- Patients with PIH experienced a statistically significant improvement in PIH after 12 weeks of use of the study cream containing 4% hydroquinone, 10% buffered glycolic acid, vitamin C, vitamin E, and sunscreen (Glyquin®, ICN Pharmaceuticals).
  - Demonstrated with both objective mexameter readings and patient/physician assessment of clinical improvement
- The study cream was safe and well-tolerated.
- In prior studies, the combination of 4% hydroquinone (which inhibits the conversion of L-dopa to melanin), 10% buffered glycolic acid, vitamin C, vitamin E, and sunscreen has been proven successful in depigmenting epidermal melasma of the face.[5,10]
- In this formulation, glycolic acid may reduce the thickness of the stratum corneum barrier, thereby enhancing the penetration of hydroquinone.
- Vitamins C and E may reduce UV-induced free radicals and decrease skin damage via an antioxidant effect.
- In the future, compounds containing even stronger moisturizers (such as hyaluronic acid) as well as sunscreens may be shown to be even less irritating with equal efficacy in the treatment of disorders of hyperpigmentation.

CONCLUSIONS

- The study cream containing 4% hydroquinone, 10% buffered glycolic acid, vitamin C, vitamin E, and sunscreen is effective in decreasing Postinflammatory Hyperpigmentation on target areas on the face and body in patients with Fitzpatrick skin types IV-VI.
- The study cream is safe and well-tolerated.

REFERENCES

1. Sriprachya-anunt S, Marchell NL, Fitzpatrick RE, Goldman MP, Rostan EF. Facial resurfacing in patients with Fitzpatrick skin type IV. *Lasers Surg Med.* 2002;30(2):86-92.
2. Lent WM, David LM. Laser resurfacing: a safe and predictable method of skin resurfacing. *J Cutan Laser Ther.* 1999;1(2):87-94.
3. Chung WH, Wang CM, Hong HS. Allergic contact dermatitis to temporary tattoos with positive para-phenylenediamine reactions: report of four cases. *Int J Dermatol.* 2001;40(12):754-756.
4. Freedberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SI. *Fitzpatrick's Dermatology In General Medicine.* 6th ed. Maidenhead, UK: McGraw-Hill Professional; 2003.
5. Guevara IL, Pandya AG. An assessment of the safety and efficacy of a cream containing 4% hydroquinone, 10% buffered glycolic acid, vitamins C and E, and sunscreen versus a cream containing sunscreen only in depigmenting epidermal melasma of the face. Poster presented at: Annual Meeting of American Academy of Dermatolog; February 24-27, 2002, New Orleans, LA.
6. Berardesca E, Distante F, Vignoli GP, Oresajo C, Green B. Alpha hydroxyacids modulate stratum corneum barrier function. *Br J Dermatol.* 1997;137(6):934-938.
7. Dreher F, Gabard B, Schwindt DA, Maibach HI. Topical melatonin in combination with vitamins E and C protects skin from ultraviolet-induced erythema: a human study in vivo. *Br J Dermatol.* 1998;139(2):332-339.
8. Tucker SC, Yell JA, Beck MH. Allergic contact dermatitis from sodium metabisulfite in Trimovate® cream. *Contact Dermatitis.* 1999;40(3):164.
9. Evans DJ, Coulby LJ, O'Connor BJ. Effect of allergen challenge on airway responsiveness to histamine and sodium metabisulphite in mild asthma. *Thorax.* 1996;51(12):1185-1191.
10. Lim JT, Tham SN. Glycolic acid peels in the treatment of melasma among Asian women. *Dermatol Surg.* 1997;23(3):177-179.

Research supported by an unrestricted educational grant from ICN Pharmaceuticals, Inc. Presented at the American Academy of Dermatology (AAD) Summer Meeting; July 25-29, 2003; Chicago, IL. Poster #37