Treatment of Mild or Moderate Melasma in Darker Skin with a 4% Hydroquinone Skin Care System Plus 0.025% Tretinoin Cream

Pearl Grimes, MD
Vitiligo and Pigmentation Institute of Southern California
Los Angeles, CA

JoAnne Watson, DPM
OMP, Inc.
Long Beach, CA

Funded by OMP, Inc.
Conflicts of Interest

• Dr Grimes – investigator and consultant for OMP, Inc.
• Dr Watson – employee of, and holds stock and stock options in, OMP, Inc.
Purpose

- To evaluate the efficacy and tolerability of treating melasma in darker skin using a 4% hydroquinone skin care system plus 0.025% tretinoin cream

[This regimen treats melasma and provides a complete skin care routine]
Rationale for Study

• Melasma can cause great distress with significant negative effects on a patient’s:
  – Emotional well being
  – Social life
  – Quality of life

• It is NOT merely a cosmetic nuisance – such misperceptions have resulted in underdiagnosis and undertreatment

• Hydroquinone and tretinoin are both effective in treating melasma and their use:
  – In combination facilitates faster improvements
  – As part of a comprehensive skin care system may offer additional advantages in terms of convenience, efficacy, and tolerability

• Optimal tolerability is especially important in darker skin to minimize the potential for other pigmentary problems
Inclusion Criteria

• 25- to 65-year old females with:
  – Mild or moderate epidermal melasma (covering 11% to 40% of face), confirmed by Wood’s lamp examination
  – Minimal to marked intensity of melasma pigmentation
  – Cutaneous melanosis stable over preceding 3 months
  – Fitzpatrick skin type III-VI
Study Design

- Patients used a 4% hydroquinone skin care system + tretinoin 0.025% cream on their face every day for up to 24 weeks (initial 12 weeks + optional 12-week extension)
## Components of 4% Hydroquinone Skin Care System

<table>
<thead>
<tr>
<th>Component</th>
<th>Key Ingredients</th>
<th>Potential Effect</th>
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<tbody>
<tr>
<td>Foaming gel cleanser</td>
<td>Aloe barbadensis leaf juice</td>
<td>Soothing and anti-inflammatory activity</td>
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</table>
| Toner                          | Aloe barbadensis leaf juice + witch hazel | Soothing and anti-inflammatory activity  
Scavenging activity against active oxygen  
Suppression of UV-induced erythema       |
| 4% hydroquinone                | Hydroquinone                      | Reduction in pigmentation                                                          |
| Exfoliation enhancer           | Glycolic acid + lactic acid       | Exfoliation                                                                       |
| Sunscreen SPF 35               | Zinc oxide + octinoxate           | Physical + chemical sunscreen                                                     |
Treatment Regimen

4% hydroquinone skin care system, consisting of 6 proprietary products:

1. Foaming gel cleanser (contains aloe barbadensis leaf juice)
2. Toner (contains aloe barbadensis leaf juice and witch hazel)
3. 4% hydroquinone
4. Exfoliation enhancer (contains glycolic acid and lactic acid)
5. Sunscreen SPF 35
6. 4% hydroquinone (different formulation to above)

0.025% tretinoin cream

Plus, as needed:

Moisturizer for dryness
0.5% hydrocortisone for other tolerability issues
Potential Advantages of Treatment Systems

• Convenient
  – Provide medical treatment and overall skin care in one regimen, saving confusion juggling different regimens

• Popular with patients

• May enhance compliance

• May enhance efficacy:
  – Cleansing and exfoliating may help penetration of other ingredients into skin
  – Sunscreen may help maintain efficacy of treatment

• May enhance tolerability:
  – May contain agents with soothing and anti-inflammatory properties (eg, aloe barbadensis leaf juice and witch hazel)

¹ Bowe et al. Semin Cutan Med Surg 2008
Investigator Evaluations

- Melasma severity
- Pigmentation intensity
- Melasma area and severity index (MASI)
- Melasma improvement
- Erythema, dryness, peeling
Patient Evaluations

- Improvement in photodamage-related parameters:
  - Skin texture/roughness
  - Skin firmness
  - Brown spots/dyschromia
  - Fine lines and wrinkles

- Quality of life:
  - Embarrassment/self-consciousness due to skin
  - Focus by others on skin discoloration
  - Feeling unattractive due to skin
  - Effort put into hiding skin discoloration
  - Social/leisure activities affected by skin

- Effectiveness of treatment compared with other medications
- Satisfaction with effectiveness of treatment
- Ease of application
- Burning/stinging
Results

• 20 females enrolled:
  – 100% (20/20) completed initial 12-week study
  – 90% (18/20) completed extension study to 24 weeks
  – 2 discontinued due to voluntary withdrawal
• Mean of 50 years old
• 65% black/African American + 35% white/Caucasian
• Fitzpatrick skin type:
  – IV (40%)
  – V (40%)
  – VI (20%)
• Melasma was:
  – Malar in 65%
  – Centrofacial in 35%
Melasma Severity

** Median grade for melasma severity**

** Scale**
- None (0)
- Minimal/trace (1)
- Mild (2 or 3)
- Moderate (4 or 5)
- Marked (6 or 7)
- Severe (8)

** Week**

** ** P ≤ .01, *** P ≤ .001 versus baseline
Pigmentation Intensity

Median grade for pigmentation intensity

Scale
- None (0)
- Minimal (1)
- Mild (2 or 3)
- Moderate (4 or 5)
- Marked (6 or 7)
- Severe (8)

*** P≤.001 versus baseline
MASI Score
(Melasma Area and Severity Index)

Median MASI score

Week

*** P≤.001 versus baseline
Improvement in Melasma

- At least 1-grade improvement in melasma severity:
  - Week 4: 47%
  - Week 8: 70%
  - Week 12: 80%
  - Week 18: 75%
  - Week 24: 67%

- At least 1-grade improvement in melasma pigmentation intensity:
  - Week 4: 74%
  - Week 8: 75%
  - Week 12: 85%
  - Week 18: 85%
  - Week 24: 78%

- Marked (≥ 51%) improvement in melasma:
  - Week 4: 16%
  - Week 8: 40%
  - Week 12: 60%
  - Week 18: 70%
  - Week 24: 72%
Patients with rating of good, very good, or excellent improvement (%)

Patient-Reported Improvements in Photodamage-Related Parameters at Week 24

- **Skin texture/roughness**: 76% (70% Good, 6% Very good, 0% Excellent)
- **Skin firmness**: 69% (48% Good, 21% Very good, 10% Excellent)
- **Brown spots/discholoration**: 65% (52% Good, 11% Very good, 12% Excellent)
- **Fine lines and wrinkles**: 59% (42% Good, 10% Very good, 7% Excellent)
Improvement in Quality of Life Parameters

Patients rating parameter as “very much” or “a lot” (%)

- Embarrassed/self-conscious due to skin: Baseline 80%, Week 4 47%, Week 12 20%, Week 24 18%
- Feeling unattractive due to skin: Baseline 80%, Week 4 42%, Week 12 35%, Week 24 35%
- Effort put into hiding skin discoloration: Baseline 90%, Week 4 58%, Week 12 37%, Week 24 37%
- Focus on skin discoloration by others: Baseline 55%, Week 4 37%, Week 12 15%, Week 24 12%
- Social/leisure activities affected: Baseline 50%, Week 4 42%, Week 12 20%, Week 24 18%
Patient Ratings at Week 24

- **Study treatment more effective than other medications**: 75%
  - Much more effective: 60%
  - More effective: 15%

- **Satisfied with overall effectiveness of treatment**: 80%
  - Very satisfied: 45%
  - Satisfied: 35%

- **Study treatment easy to apply**: 81%
  - Very easy: 65%
  - Easy: 16%
Improvement in Melasma
Improvement in Melasma
Efficacy Summary

• Treating melasma with the 4% hydroquinone skin care system + 0.025% tretinoin was associated with:
  – Significant improvements in melasma
    • Less severe melasma (P≤.01 from week 4 onward)
    • Less intense pigmentation (P≤.001 from week 4 onward)
    • Lower MASI score (P≤.001 from week 4 onward)
  – High levels of patient satisfaction
  – Considerable improvements in quality of life
    • Less embarrassment/self-consciousness
    • Less feeling of being unattractive
    • Less effort hiding skin discoloration
    • Less focus from other people on the melasma
    • Less effect on social and leisure activities
  – Good improvements in photodamage-related parameters:
    • Skin texture
    • Skin firmness
    • Brown spots/discholoration
    • Fine lines and wrinkles
Adverse Events

• 4 patients had adverse events at least probably related to treatment:
  – Erythema
  – Erythema/dryness
  – Dryness/peeling
  – Erythema/dryness/stinging sensation

• All were mild except erythema was moderate in 1 patient
Tolerability

• Erythema, dryness, peeling, and burning/stinging (evaluated up to week 12 only):
  – Mean grades between “none” and “trace” at all timepoints
  – Median grades “none” at all timepoints
  – Only significant change from baseline was ↑ erythema at week 12

• 17/20 (85%) patients used the study moisturizer:
  – 0 as treatment for dryness
  – 17 as preventive measure

• 3/20 (15%) patients used hydrocortisone:
  – 1 for erythema/stinging sensation
  – 3 as preventive measure
Conclusion

• Using the 4% hydroquinone skin care system + 0.025% tretinoin cream to treat epidermal melasma in darker skin can achieve significant reductions in:
  – Melasma severity
  – Melasma pigmentation intensity
  – Melasma area and severity index

• Importantly, treatment is also associated with considerable improvements in:
  – Quality of life
  – Signs of photodamage (eg, skin roughness, fine lines/wrinkles)

• Treatment is well tolerated and associated with a high level of patient satisfaction