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

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

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

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

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 patients¹
• May enhance compliance¹
• 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)

** P≤.01, *** P≤.001 versus baseline
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
At least 1-grade improvement in melasma pigmentation intensity
Marked (≥51%) improvement in melasma

Week: 4 8 12 18 24
47% 70% 80% 75% 67%
74% 75% 85% 85% 78%
16% 40% 60% 70% 72%

Patients (%)
Patient-Reported Improvements in Photodamage-Related Parameters at Week 24

- **Skin texture/roughness**: 76% of patients rated their improvement as good, very good, or excellent.
- **Skin firmness**: 69% of patients rated their improvement as very good.
- **Brown spots/dyscoloration**: 65% of patients rated their improvement as very good.
- **Fine lines and wrinkles**: 59% of patients rated their improvement as very good.
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 18%, Week 24 18%
- Effort put into hiding skin discoloration: Baseline 90%, Week 4 58%, Week 12 37%, Week 24 35%
- 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)
- Satisfied with overall effectiveness of treatment: 80% (Very satisfied)
- Study treatment easy to apply: 81% (Very easy)
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/discoloration
    - 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 \( \uparrow \) 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