Treatment of hyperpigmentation in darker skins

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I have no financial or other relationships that might lead to a conflict of interest
Agenda

- The **characteristics** of skin of color
- The **problems** of skin of color
- The **treatment options** for localized hyperpigmentation
  - Melasma
  - Postinflammatory hyperpigmentation
Fitzpatrick skin classification / Skin of color
Skin of color / Hyperpigmentation

- Higher content of melanin
- Higher eumelanin / feomelanin
- 😊 Protection against UV radiation
- 😞 Postinflammatory dyspigmentation

- One of the most common skin complaints ~ 10%
- Management is often challenging

## Acquired hyperpigmentation in skin of color

<table>
<thead>
<tr>
<th>Acquired hyperpigmentation</th>
<th>Melasma</th>
<th>Phytophotodermatitis</th>
<th>Periorbital hyperpigmentation</th>
<th>Cervical poikiloderma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postinflammatory hyperpigmentation</td>
<td>Dermatosis papulosa nigra</td>
<td>Flagellate dermatosis</td>
<td>Primary cutaneous amyloidosis</td>
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<tr>
<td>Acanthosis nigricans</td>
<td>Erythema dyschromicum perstans</td>
<td>Confluent and reticulated papillomatosis of GC</td>
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</tbody>
</table>
Before the treatment

- **Identify** and **treat** any underlying dermatosis (SD, etc.) or contributing factors
  - ✓ Aggressive pigmentary therapeutics!!
- **Rational treatment goals**
- Keep an open mind for **multi-therapy** approach
- **Sun protection** must be central
  - Sunscreens, pref. **physicals** on all sun-exposed skin
  - Physical barriers, hats and clothing

Melasma

Melasma

- Current treatments available remain unsatisfactory

- Topical combination therapies are more effective
  - ✓ Triple combination is most effective
    - 😞 40% erythema and peeling

- Chemical peels

- Laser and light therapies have mixed results
  - 😞 Increased risk of irritation and PIH

Postinflammatory hyperpigmentation (PIH)
PIH

- Firstly, aim to treat underlying disorders

- It often takes months

- Topical therapy is typically effective for epidermal PIH

- Chemical peeling and lasers may help in recalcitrant hyperpigmentation.

- All treatments should be used with caution to prevent irritation and worsening of PIH

### Table 2: Skin-lightening agents. Adapted from [52].

<table>
<thead>
<tr>
<th>Mechanism of action</th>
<th>Compound</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tyrosinase inhibition</strong></td>
<td>Arbutin</td>
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<tr>
<td></td>
<td>Azelaic acid</td>
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<tr>
<td></td>
<td>DeoxyArbutin</td>
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<tr>
<td></td>
<td>Glycolic acid</td>
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<tr>
<td></td>
<td><strong>Hydroquinone</strong></td>
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<td></td>
<td>Liquorice extract</td>
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<tr>
<td></td>
<td>Mequinol</td>
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<tr>
<td></td>
<td>N-Acetylglucosamine</td>
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<tr>
<td></td>
<td>N-Acetyl-4-S-cysteaminyphenol</td>
</tr>
<tr>
<td>Reduction in melanosome transfer</td>
<td>Niacinamide</td>
</tr>
<tr>
<td></td>
<td>Retinoids</td>
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<tr>
<td></td>
<td>Soybean trypsin inhibitor</td>
</tr>
<tr>
<td>Interaction with copper</td>
<td>Ascorbic acid</td>
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<tr>
<td></td>
<td>Kojic acid</td>
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<tr>
<td>Stimulation of keratinocyte turnover</td>
<td>Glycolic acid</td>
</tr>
<tr>
<td></td>
<td>Retinoids</td>
</tr>
<tr>
<td>Inhibition of melanosome maturation</td>
<td>Arbutin</td>
</tr>
<tr>
<td></td>
<td>DeoxyArbutin</td>
</tr>
<tr>
<td>Inhibition of protease-activated receptor 2</td>
<td>Soybean trypsin inhibitor</td>
</tr>
<tr>
<td>Oxidation and breakdown of melanin</td>
<td>Lignin peroxidase</td>
</tr>
</tbody>
</table>

# Skin lightening preparations and the hydroquinone controversy

**ZOE DIANA DRAELOS**

Department of Dermatology, Wake Forest University School of Medicine, Winston-Salem, North Carolina and Dermatology Consulting Services, High Point, North Carolina

## TABLE 1. General treatment guidelines

<table>
<thead>
<tr>
<th><strong>FIRST-LINE THERAPY</strong></th>
<th><strong>SECOND-LINE THERAPY</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Topicals with triple combination therapy (including hydroquinone, topical retinoids, topical steroids)</strong></td>
<td><strong>Chemical peels in combination with topicals</strong>&lt;br&gt;  • Salicylic acid peels may help with concomitant acne &lt;br&gt;  • Studies show some data favoring glycolic acid peels</td>
</tr>
<tr>
<td>Topicals, such as zinc sulfate, arbutin, azelaic acid, kojic acid; some cosmeceuticals can be added as a second topical, but can be tried as monotherapy</td>
<td>Laser therapy&lt;br&gt;  • Pay particular attention to skin type, laser fluence, and type&lt;br&gt;  • Recent studies show benefits with Q-switched Nd:YAG</td>
</tr>
<tr>
<td>Should patients develop irritation/allergy to triple combination therapy, dual combinations can be used (either due to a retinoid dermatitis or hydroquinone sensitivity)</td>
<td></td>
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</tbody>
</table>
• Little controlled studies

• The therapy with highest evidence (First-line)
  Fixed TC
  Hydroquinone 4%
  Tri-Luma (Galderma)
  Tretinoine 0.05%
  Flucinolonaetonide 0.01%

  *If allergy or irritation to TC, Dual Combinations

• Second-line
  * TC + peels or microdermabrasion
  ** Lasers and light sources
Hydroquinone

- Few controlled studies
- Effective in 2% - 5%
- Irritation
- Contact allergy
- Exogenous ochronosis
- Carcinogenic?
- Sold with prescription

- Kligman’s Hydroquinone 5%
  Tretinoine 0.1%
  Dexamethasone 0.1%

Fixed TC & Hydroquinone 4% in melasma

- Multicenter, randomized, controlled 8-week trial
- Fixed TC (n=129), hydroquinone (n=131) Asian patients
- Assessment of MASI, GSS, patient satisfaction

- TC has superior efficacy (64.2% & 39.4%)
- For all parameters
  Fixed TC > Hydroquinone
- TC was associated with more adverse effects, mostly mild!!

Skin lightening agents - Use or abuse? - A retrospective analysis of the topical preparations used by melasma patients of darker skin types

Rajat Kandhari, Niti Khunger
Department of Dermatology and STD, V. M. Medical College and Safdarjang Hospital, New Delhi, India

- 69 melasma patients with skin of color
- Topically treated > 3 months
Tazarotene & Adapalene in PIH

- 16-week trial on patients with moderate to severe acne
- Once daily Tazarotene 0.1% cream & Adapalene 0.3% gel
- Assessments of reduction of acne lesions and PIH
- Tazarotene has superior efficacy, also in reduction of PIH
- Irritation was mild and similar in two groups

Newers: Methimazole in melasma

- A potent peroxidase inhibitor
- Important in final steps of melanogenesis
- Not melanocytotoxic

A. Hydroquinone resistant melasma
B. After 2 months

Newers: 4-n-butylresorcinol

- High inhibitory capacity on human tyrosinase activity
- Exceeds by far the potency of hydroquinone, arbutin and kojic acid

Figure 2. Inhibition of melanin production in MelanoDerm™ skin models by 4-butylresorcinol, kojic acid, arbutin and hydroquinone.

Figure 4. Clinical Study – monitoring of a treated age spot during treatment with a spot applicator. Photographs of age spots

Newers: Decapeptide-12 in PIH

- A potent tyrosinase inhibitor
- Not melanocytotoxic

**FIGURE 1.** Before and after digital photographs demonstrating marked improvement of PIH after combined treatment with topical and dermalinfused decapeptide-12 for 8 weeks.

Chemical peels in skin of color

- Superficial peels are generally effective
- Deep peels should be avoided (PIH!)
- Pretreatment with a course of hydroquinone may improve
- Topical retinoids should be stopped before 7 days

- Standard options
  - Glycolic acid 10-70%
  - Salicylic acid 20-30%
  - TCA 10-25%
  - Jessner’s solution

- Newers
  - Tretinoin
  - Pyruvic acid
  - B-lipohydroxy acid
  - Mandelic acid
  - Amino fruit acids

Glycolic acid and salicylic acid

- Both peels have shown beneficial for melasma and PIH
- Five salicylic acid peels 20-30% with 2-week interval for PIH 
  80% of patients with skin of color (n=5) had >75% improvement
- Eight glycolic acid peels 10-30% with 2-week interval
  Useful for superficial scarring and melasma

Glycolic acid (GA) & amino fruit acid (AFA)

- Both of them are effective
- AFA peel was better tolerated

TCA & QS-Nd:YAG Laser

**TABLE 2. The Mean of the Improvement Percentage of MASI Score Among Different Study Groups**

<table>
<thead>
<tr>
<th>Study Groups</th>
<th>Mean Improvement Percentage, Mean ± SD (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (TCA 20%)</td>
<td>39.9 ± 20.7 (28.5 to 51.4)</td>
<td>&lt;.001***</td>
</tr>
<tr>
<td>Group 2 (TCA 25%)</td>
<td>64.7 ± 21.9 (54.4 to 74.9)</td>
<td></td>
</tr>
<tr>
<td>Group 3 (TCA 30%)</td>
<td>24.7 ± 33.3 (6.2 to 43.1)</td>
<td></td>
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<tr>
<td>Group 4 (QS-Nd:YAG)</td>
<td></td>
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<tr>
<td>532 nm</td>
<td>−49.2 ± 66.3 (−85.9 to −12.4)</td>
<td></td>
</tr>
<tr>
<td>1,064 nm</td>
<td>−83.6 ± 86.8 (−163.8 to −3.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>−19.1 ± 11.0 (−28.2 to −9.9)</td>
<td></td>
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</tbody>
</table>

The negative signs indicate worsening of melasma and higher MASI score after treatment. ***Highly statistically significant.

DISCUSSION

- TCA 25% is most effective
- QS-Nd:YAG (532 nm) has highest complications

TCA & QS-Nd:YAG Laser

8 sessions with TCA %25 peeling

TCA & QS-Nd:YAG Laser

6 sessions with QS-Nd:YAG laser (532 nm), monthly.

Lasers / light sources in skin of color

- Lasers are last options for recalcitrant cases
- In selected ones, with great caution
- The **safest** and efficient laser
  QS-Nd:YAG laser with its longer wave length (1064 nm)
- QS-Ruby laser 694 nm is **not recommended** in darker skin
- IPL has **mixed** results

Low fluence QS-Nd:YAG Laser 1064 nm

- n=22 Thai patients
- Spot size: 6 mm; Fluence: 3.0-3.8 j/cm² (not very low?)
- 5 sessions with 1-week interval (short interval?)
- Only temporary improvement
- 4/22 rebound hyperpigmentation
- All had recurrence of melasma

A. Baseline  
MASI (R)=21  
MASI (L)=22  

B. After laser  
MASI (R_laser)=4  
MASI (L_topical)=14  

C. FU, 1 month later  
R=rebound
Low fluence QS-Nd:YAG Laser 1064 nm

- n=20 Korean patients
- Spot size: 6 mm;
- Fluence: 2.0-3.5 j/cm²
- 5 sessions, 1-week interval

Low fluence QS-Nd:YAG Laser 1064 nm

5 sessions, fluence: 2.0-3.5 j/cm², 1-week interval

Low fluence QS-Nd:YAG Laser 1064 nm

- n=25 Korean patients
- Spot size: 6 mm; Fluence: 2.0-3.5 j/cm²
- 5 sessions with 2-week interval
- 18/25 patients were satisfied (50-100% improvement)

Low fluence QS-Nd:YAG Laser 1064 nm

5 sessions, fluence: 2.0-3.5 j/cm², 1-week interval

Low fluence QS-Nd:YAG 1064 nm

After 5 sessions

• PIP-IPL may be a safe and promising treatment

PIP-IPL & IPL + QS-Nd:YAG Laser

A: PIP-IPL
B. IPL + QS-Nd:YAG

FU: 6 months with hydroquinone 4%

1410 nm Fractional Photothermolysis Laser

- It is safe and **temporary** effective, but long-term follow-up is still needed
- Only **5%** coverage should be used to minimize risks

![Images of treatment with captions](image)

(a) Pretreatment, b. 1 month after 5 sessions, c. 2 weeks after PIH

1550 nm Fractional Photothermolysis Laser

3 sessions with 4-8 weeks interval, 7 months after the last session

Fractional CO$_2$ Laser

Figure 1. Postinflammatory hyperpigmentation before treatment

Figure 2. Total clearance of postinflammatory hyperpigmentation one month after two treatment sessions of fractional CO$_2$ laser

Take home messages

• Identify and treat any underlying and / or contributing factors
• Rational treatment goals
• Keep an open mind for multi-therapy approach
• Sun protection must be central

• First-line therapy: Topicals with TC or newers
• Second-line therapy: Chemical peels with topicals
• Laser and light therapies:
  Special attention for type, skin type, fluence
  More benefits with low fluence QS-Nd:YAG