Melasma: Differential Diagnosis and Treatment with Tranexamic Acid

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Disclosure of relationships with industry

None

Melasma
- Common
- Affected by hormones—pregnancy and oral contraceptives
- May fade post-partum
- More common in brown races
- 90% are women
- Worsened by UVB and UVA light
- Psychologically distressing
- Distinct morphology

Hori Nevus (ABNOM)
- Acquired Bilateral Nevus of Ota-Like Macules (Hori’s nevus)
  - More common in Eastern Asians
  - Affects 4.2% of Chinese women
  - Due to dermal melanocytes
  - Responds to laser surgery
  - Macules tend to be smaller than melasma
  - Often with blue-gray color
  - Usually on cheeks only

Melasma- Differential Diagnosis
- Post-inflammatory hyperpigmentation
- Lentigines
- Hori nevus
- Drug-induced hyperpigmentation
- Lichen planus pigmentosus
- Acanthosis nigricans
- Periorbital dark circles
- Pigmentary demarcation lines

Visible Light May Cause Melasma
- 20 volunteers tested on back
  - Visible (400-700 nm)
  - UVA1 (340-400 nm)
- BOTH induced immediate and delayed hyperpigmentation in skin type 5
- Currently available sunscreens inadequate


**Sunscreen with Iron Oxide May Help Patients with Melasma**

- Study with 20 subjects evaluated after ALA applied to arm
- Different sunscreens applied prior to visible blue light exposure
- Results: Minimal phototoxic dose (MPD) 18 hours post ALA

<table>
<thead>
<tr>
<th>Sunscreen</th>
<th>MPD (J/cm²)</th>
<th>Protection Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control—(No sunscreen)</td>
<td>0.33</td>
<td>0</td>
</tr>
<tr>
<td>A—titanium dioxide 11%, zinc oxide 2.4%, iron oxide 0.2% (Avene cream, SPF 50)</td>
<td>0.81</td>
<td>2</td>
</tr>
<tr>
<td>B—titanium dioxide 15%, zinc oxide 6.8%, iron oxide 3.2% (Avene compact paste, SPF 50)</td>
<td>5.78</td>
<td>21</td>
</tr>
</tbody>
</table>


**A Sunscreen Against Visible Light Helps Patients with Melasma**

- 68 patients with MASI > 8
  - UV-only sunscreen with Mexoryl
  - UV + visible light sunscreen with iron oxide
- Application every 2-3 hrs x 8 wks
- All received HQ 4%
- Improvement in MASI
  - 77.8 ± 11% for visible group
  - 61.9 ± 16% for UV-only group (p < 0.001)
- Biopsies: Melanin significantly lower in visible group


**Hydroquinone**

- 40% of patients clear or almost clear with 4% HQ after 3 months
- Penetration MAY be increased with tretinoin and glycolic acid
- Response in 4-6 weeks, maximum in 3-6 months or longer
- Irritation and ochronosis rare
- Exogenous ochronosis more common with high concentrations, lack of supervision or combination with resorcinol


**Tranexamic Acid**

- Plasmin inhibitor and antifibrinolytic
- FDA approval in 2009 for menorrhagia
- Over the counter in some countries (UK, Sweden)
- Also-used for intraoperative and trauma-related hemorrhage
- Used widely for melasma in East Asia (Japan, Korea, Singapore)
- Topical, intradermal and oral forms – latter potent and convenient

Tranexamic Acid for Menorrhagia

- Recommended oral dosage is 2 pills, 650mg each, three times daily for up to 5 days.
- Maximum total dose of 20g/month (dose for melasma: 15g/month)
- Contraindications:
  - Active thromboembolic disease
  - History of thrombosis or thromboembolism
  - Intrinsic risk for thrombosis or thromboembolism
- Pregnancy category B drug

Int. J. Women’s Health. 2012; 4:413-21

Retrospective Review of Tranexamic Acid in 561 Patients With Melasma

- Retrospective review of 561 patients in Singapore
- 91% female
- Dosed at 250 mg bid
- 91.7% improved
- Mean response in 2 months
- 7.1% with adverse effects
- 1 thrombotic event in a patient with protein S deficiency and a family history of thrombotic events who withheld history and developed a DVT
- Better results in those with older age of onset and longer duration of disease

Chee Leok Goh, MD, MRCP et al. JAAD May 2016

Summary- Tranexamic Acid for Melasma

- Over 12 studies (> 1600 patients) published, all from Asia, all but one uncontrolled
- Dose is usually 250 mg bid (lower than menorrhagia dose)
- Treatment duration 1-4 months
- Causes moderate improvement, based on MASI scoring
- Side effects are rare
- Contraindications: history of deep venous thrombosis, stroke, other thrombotic events, hypercoagulable states, use of anticoagulants, 2 or more spontaneous abortions, pregnancy, nursing
- Relative contraindications: family history of DVT

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