Melasma: Treatment with Tranexamic Acid, Peels and Laser

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Disclosure of relationships with industry

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F016 – Pigmentary Therapeutics
DISCLOSURES
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

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: 15 g/month)
- Contraindications
  - Active thromboembolic disease
  - History of thrombosis or thromboembolism
  - Intrinsic risk for thrombosis or thromboembolism
  - Pregnancy category B drug
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

Glycolic Acid Peels + Modified Kligman’s Formula for Melasma

- 40 women from India treated with serial peels + modified Kligman’s formula (MKF) vs. MKF alone for 5 months
- MKF: 2% HQ + 0.05% tretinoin cream + 1% hydrocortisone cream
- Six serial glycolic acid (GA) peels to half the patients every 3 weeks
- First 3 peels 30% GA and last 3 peels 40% GA
- Maximum time of contact was 3 minutes
- Subjective scoring methods
- Improvement in MASI
  - Peels + MKF
  - MKF alone
  - 12 weeks 45.9% 33.2%
  - 21 weeks 80% 63.1%
- Tolerated well

Randomized, Split-Face, Investigator Blinded, Controlled Trial with Glycolic Acid Peels for Melasma

- 20 Hispanic women
- Twice daily 4% hydroquinone
- Four serial glycolic acid peels to one side of the face every 2 weeks
- First 2 peels 20% GA and last 2 peels 30% GA
- Results:
  - Both sides improved significantly
  - Both mexameter and MASI results showed NO SIGNIFICANT DIFFERENCE between both sides

Hurley ME, Pandya AG, et al., Arch Dermatol 2002; 138:1578

Randomized, Split-Face, Investigator Blinded, Controlled Trial with Salicylic Acid Peels for Melasma

- 20 patients
- Hydroquinone 4% cream to both sides of face
- Four salicylic acid peels, once every 2 weeks to one side of face
- First 2 peels- 20% SA, second two peels- 30% SA
- 8 week follow up period
- Results:
  - Both sides improved
  - Both mexameter and MASI scores showed NO SIGNIFICANT DIFFERENCE between both sides

**Triple Combination Cream + PDL for Melasma**
- Dual treatment designed to target melanin and vasculature
- 17 patients, treated with TC cream daily for 4 months
- PDL applied every 3 weeks to 3 sessions to one side of face
- MASI scores:

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>End of Treatment</th>
<th>End of Summer (&gt;2 months post treatment)</th>
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</thead>
<tbody>
<tr>
<td>Cream alone</td>
<td>6.76</td>
<td>4.35</td>
<td>6.06</td>
</tr>
<tr>
<td>Cream + PDL</td>
<td>6.20</td>
<td>2.79</td>
<td>4.15</td>
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- Only phototypes II and III improved, phototype IV unchanged


**IPL + TC Cream for Melasma**
- 56 patients from USA treated for 10 weeks
- ½ of face treated with TC cream and ½ with control cream
- Two sessions of IPL (filter 560 nm and fluence of 14-18 J to skin phototypes II–IV) at weeks 2 and 6 to the whole face
- Creams discontinued one day before to one day after IPL
- Photos at baseline, week 6 and week 10
- 57% were clear or almost clear on combination side vs. 23% on IPL only side
- Well tolerated


**Low-fluence Q-switched Nd:YAG laser for melasma in Asians (Laser Toning)**
- Split-face study: Q switched Nd:YAG laser + 2% hydroquinone vs. 2% hydroquinone alone
- Parameters: 1,064-nm Q switched Nd:YAG laser, 6-mm spot size, 3.0- to 3.8- J/cm² fluence (sub photothermolysis)
- One session every week for 5 weeks
- Results: 53% colorimeter and 49% MASI improvement on laser side compared to 20% and 24%, respectively, on control side
- 12 weeks follow up, 4/22 patients had rebound hyperpigmentation and there was at least mild recurrence of melasma in all patients despite use of 2% HQ and sunscreens
- Mottled hypopigmentation in 4 patients with darker skin (type V)


**Melasma Treatment Algorithm**
- **Acute**
  - Hydroquinone
  - Triple combination cream
  - Compounded cream
  - Tranexamic acid
  - Peels?
  - Laser?
- **Maintenance**
  - 2% hydroquinone
  - Triple combination cream
  - 2-3 X per week
  - Kojic acid
  - Azelaic acid
  - Arbutin
  - Combination

**Conclusions**
- Rule out other causes of facial pigmentation
- Sunscreens against UVA and UVB are critical for success
- Sunscreens against visible light may also be important
- Hydroquinone is still the most effective depigmenting agent
- Triple combination cream is effective in the majority of patients
- Tranexamic acid shows promise in treating melasma without significant side effects
- Close follow-up of patients is important to avoid side effects
- Most patients need long-term treatment