Efficacy and safety of lasers and light-based therapy for melasma

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Conflicts of interest

- Research grants and/or honoraria:
  - Bioderma
  - Beiersdorf
  - DELEO
  - Galderma
  - L’OREAL
  - ISIS Pharma
  - SVR
  - Symrise
  - Syneron-Candela

Melasma is a long-lasting disorder

- Spontaneous improvement during winter
- High rate of recurrences (after summer+++)

Role of the visible light

- Visible light induces significant and long-lasting hyperpigmentation in dark skin types (skin types III and higher)
- Only the shorter wavelengths of the visible light are propigmenting
- Mechanisms involved appear to be different to those involved in UVB-induced pigmentation

Impact of protection against shorter wavelengths of visible light in melasma relapses

- Monocentric randomized comparative study on 40 patients with melasma
- Begin of the study the two first weeks of April
- End of the study the two first weeks of September
- Evaluation on MASI performed on standardized pictures (VISIA, Canfield) by two independent physicians blinded to the sunscreen received

- No lost to follow-up
- No significant differences in the quantity of sunscreen used

- In mean MASI score between last and first visit

Laser and light-based treatments of melasma

- Q-switched rubis, alexandrite or Nd:YAG lasers:
  - Mild to moderate efficacy
  - Constant relapses and high rate of PIH

- Intense pulsed light
  - Mild to marked improvement reported in several studies
  - Combination with Trio > Trio alone
  - Decrease in MASI score remains at 44.9% at 12 months in combination group Vs none in Trio alone
  - Risk of PIH mostly in skin type IV to VI
**Low-fluence QS laser and melasma**

- Low-fluence QS 1064nm laser showed promising results in pilot studies
- Prospective randomized split face study
  - 22 patients with melasma
  - 2% HQ vs 2%HQ + low-fluence QS Nd:YAG 1064nm
  - HQ started 2 weeks before the laser treatment
  - 5 weekly sessions of laser in total (spot 6 mm; fluence 3 to 3.8 J/cm²)
- Evaluation:
  - MASI + colorimeter
  - Follow-up: 12 weeks after the end of the treatment

**Results:**
- End of Tx: ++
- At 12 weeks: Relapse in all the patients + 4 PIH

**Low-fluence QS laser side effects**

- 14 cases of hypochromia sequella following repetitive use of low-fluence QS laser (9 for photoageing and 5 for melasma)

⇒ No or weak interest of low-fluence QS laser for treating melasma

**Non ablative fractional laser for melasma**

- 1550nm fractional laser showed interesting results for treating melasma in preliminary studies
- Open study:
  - 25 patients
  - One session every month for 4 months
  - Evaluation: MASI and spectrophotometry
  - Follow-up: 6 months

**Results:**
- After Tx:
  - Marked improvement in 24% of patients
- At 6 months:
  - Constant but slight relapses
  - MASI: mean 7.6 (3.2–14.7) at M0 to 6.2 (1.8–10.2) (p=0.03)
  - Worsening of the hyperpigmentation in 13% of cases

- Prospective comparative randomized study
- 20 melasma patients, skin types II to V
- Non ablative 1550nm fractional erbium laser
  - 8 passages (MTZ 2000 to 2500/cm²; 10mJ)
  - 1 session every 2 weeks for 8 weeks
- Vs Kligman’s trio
  - 1/d for 8 weeks
  - Evaluation blinded to the treatment received
  - Main criterion: PGA
  - Follow-up 3 wks, 3 and 6 months after the end of the treatment
Both treatments are effective at 3 weeks.

No significant statistical difference between the 2 groups.

In both groups half of the patients relapsed at 6 months.

Only 8 weeks of treatment with Kligman’s trio (instead of 12 weeks).

Kligman’s trio remains the gold standard treatment for melasma!

J Am Acad Dermatol 2011;64:516-23

Laser thulium 1927 nm for melasma

Encouraging results in a pilot study in 2012.
Retrospective study in 20 women with long term follow-up.
Skin type I to IV
10-20 mJ/cm² with 60-70% coverage.
Evaluation on MASI score up to 12 months.
15 patients seen at 12 months.
Recurrence in 7 out of 15 patients.
2 PH.

One retrospective study combining Thulium and PDL.
4/11 had more than 50% of improvement.
No rebound, no PH.
No prospective randomized study available.

Revisiting melasma pathology

Increased number of melanocytes, increased epidermal and dermal melanin.

- 93% moderate/severe elastosis
- 84% increased melanocytes
- Increased melanin at all level of the epidermis
- Dermal melanin in 36% with increased dermal melanin and melanophages (12%)
- 70% moderate/severe elastosis
- No increase in melanocytes
- Melanin not increases in the epidermis
- Dermal melanin noted in 36% of perilesional cases in Korean skin

Melasma, a vascular disorder?


Vessel size (µm²)
Vessel density (mm²)
Vessel area (%)

Perilesional normal skin
Lesional skin

Factor VIIIa-related antigen
Factor VIIIa-related antigen

J Invest Dermatol 2011;131:1692-700

Melasma Transcriptomic study

Identification of genes differentially expressed in melasma

- 12 patients (only 10 evaluated)
- 279 genes significantly up or down-regulated in melasma lesional skin
- Up-regulation of many melanin bio-synthesis-related genes as well as melanocytes markers
- Increased expression of a subset of Wnt pathway modulator genes
- Prostaglandin metabolic process up-regulated
- Genes that regulate fatty and metabolism differentially expressed

=> Many cells and biological functions are involved in the pathophysiology of melasma.

J Invest Dermatol. 2011;131:1692-700
**Regulation of skin pigmentation: A complex process**

- UV
- Keratinocyte
- Fibroblasts
- Pro-Inflammatory Dermal cells
- Mitochondria

**Role of skin microvascularization in pigmentation**

- 100 benign vascular lesions
- High magnification digital dermoscopy (x50 – X200)
- Laser confocal microscopy and histology

- Significant increase of pigmentation above and around vascular lesions

**Mechanism of action of tranexamic acid in melasma?**

- Prospective study with biopsies after 12 weeks of treatment with TA

- TA might act on melasma through a decreased production of endothelin 1
**PDL treatment for melasma**

- Prospective randomized controlled slip face study
- 18 patients with melasma (skin types II to IV)
- Intervention:
  - Stabilized triple combination cream
    - Applied once a day for 4 months on the entire face
  - PDL
    - Start after 1 month of triple combination cream
    - 3 sessions (every 3 weeks) on 1 hemi face
    - 1st passage with pressure hand piece 10mm, 1.5ms, 7J/cm²
    - 2nd passage with hand piece 7mm, 20ms, 10J/cm², DCD 30/40
  - Blinded evaluation after 1 summer

**Results**

- Mean difference between the 2 groups in 'hemiMASI' score at V4 was 1.9 points (p=0.019)

![Graph showing results](image)
PDL and melasma

- Promising results
  - Need confirmation in larger series
  - Optimal parameters and schedule of treatment have to be determined


- Risk of PH in skin types IV and higher that limits this approach

> Interested of targeting vessels for treating melasma

- Risk of PIH in skin types IV and higher that limits this approach

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Melasma

- Photoprotection ++ (including against shorter wavelenghts of visible light)
- Discourage discontinuation of hormonal treatment +/-Avoid friction

- Results confirmed in a recent Korean prospective trial (IPCC 2014 Pr YH Kang) and in a recent case report with long term follow-up

- Risk of PIH in skin types IV and higher that limits this approach

- Interested of targeting vessels for treating melasma

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Success

HQ 5%
Tretinoin 0.1%
Dexamethasone acetate 0.1%

Failure

Chemical approaches to prevent visible light-induced pigmentation

Success

HQ 5%
Tretinoin 0.1%
Dexamethasone acetate 0.1%

Failure

Chemical approaches to prevent visible light-induced pigmentation