

New Approach for Laser Treatment of Melasma and Hyperpigmented Lesions

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Abstract

Melasma is one of the most common aesthetic problems in Asians and is one of the most difficult conditions to be treated. In the past result after laser treatment was usually believe to be unpredictable. This believes was based on anecdotal reports with variable laser parameters. In order to get better and long lasting result, we need to understand biology of melanin synthesis, pathogenesis of melasma, laser / light tissue reaction, sun screen and effect of whitening agents.

Keywords: Melasma; Melanin; Laser; Lesions

Melanin Synthesis

Most of melasma patients are photo skin type III to V. These skin type's response to sunlight by increasing of melanin synthesis. Melasma relates to strong sun light exposure and high estrogens. Melanins are synthesized in epidermal melanocytes and transfer to epidermal keratinocytes. One melanocyte supplies thirty six keratinocytes and is called "epidermal melanin unit". Majority of melanin granules are distributed in the keratinocytes. Melanin granules in melanocytes are mainly early stage (stages I-II) which contains less melanin. UV exposure stimulates keratinocytes to release cytokines (especially endothelins) which bind to endothelin receptors on melanocyte cell membrane. The binding of keratinocytes and melanocytes is through binding of Stem Cell Factor (SCF) on keratinocytes and C-kit protein on melanocytes. Endothelins together with Melanocyte Stimulating Hormone (MSH) stimulate tyrosinase enzymes synthesis. These enzymes are essential for melanin synthesis. Any conditions producing basement membrane injuries will lead to melanin dropping down into upper dermis. They will be engulfed by macrophages transforming to what we call "melanophages". These melanophages will persist in dermis for many years. Recently, there were many published articles on finding of increase of vascular dilatation and vascular growth factor in melasma.

In normal skin most of the mature melanins (stage V) will be in keratinocytes. Epidermal or follicular melanocytes contain unmelanized melanin (stage I-II). This unmelanized melanin will not absorb enough laser energy to produce "Selective Photothermolysis" or photomechanical destruction of melanin and also of melanocytes. The surviving melanocytes are the major source of recurrence of lesions after selective pigmented laser treatment (e.g. 532 nm frequency-doubled Q-switched Nd: YAG laser). For hyperpigmented lesions, mature melanin present in all these locations; keratinocytes, epidermal melanocytes and melanophages. In order to reduce hyperpigmentation, the treatment should be able to reduce melanin all three locations. In hyperpigmented lesions melanin granules also aggregate into clumps. This produces dark color, while small fragmented and dispersed melanin produce lighter colour [1-6].

In summation, the following mechanisms had been used with mild to moderate result for treatment of melasma:

1. Superficial peelings e.g. chemical peels, microdermabrasion, laser resurfacing.
2. Stimulation of keratinocytes turnover. Example: vitamin A acid, glycolic acid, salicylic acid.

3. Suppression of melanin synthesis. Example: hydroquinone, arbutin, kojic acid, licorice PT40, tranxemic acid etc.

4. Reduction of pigment transfer from melanocytes to keratinocytes. Example: Niacinamide, Clove extracts

5. Destruction of melanin's containing cells (melanocytes and Keratinocytes) e.g. Q-switched laser, Fractional laser

Pathogenesis

Melasma is a complex disease. The pathogenesis involves: 1) Hyperfunction of clones of epidermal and follicular melanocytes in certain sun-exposed area. 2) Increase in number of epidermal and follicular melanocytes in lesions (average 30%). 3) Presence of dermal melanophages. 4) vascular dilatation and endothelial proliferation and 4) mild chronic perivascular inflammation. The dermal melanophages will be able to survive in the dermis for many years and resisted to all topical treatments. Recently histologic study in melasma in Asians has demonstrated that, majority (more than two third) of melasma is a combination of epidermal melanocytes hyperactivity, increase in melanocytes with dermal melanophages. There is no such condition that has been called dermal melasma. If mature melanocytes are detected in the dermis, they should be classified as a condition in the group of dermal melanocytotic disorder. The most common condition in this group is acquired bilateral nevus of Ota like macules (Hori's nevus) which was found in 2% of adult Asian women and Nevus of Ota [6-15].

Treatments

Since melasma had been believed to be a hyperfunctional disorder, the accepted treatment was topical bleaching agents. The most widely used drug was hydroquinone. Other drugs e.g. Arbutin, Kojic acid, Licorice PT 40 are less popular because of lower efficacy and higher cost. The recommended concentration of hydroquinone was 2-4%. Even though hydroquinone is still the bench mark for medical

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Received August 10, 2014; **Accepted** August 22, 2014; **Published** August 24, 2014

Citation: Polnikorn N (2014) New Approach for Laser Treatment of Melasma and Hyperpigmented Lesions. Pigmentary Disorders 1:128. doi:10.4172/JPD.1000128

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treatment of melasma it has created many problems. One of the most common problem after prolong using of hydroquinone is rebound hyperpigmentation and cutaneous toxicity (e.g. ochronosis) both are common in Asians. Combination of hydroquinone with retinoic acid and steroid (Kligman's formula: 5%Hydroquinone + 0.05%retinoic acid + 0.1%dexamethasone) increases effectiveness but also increases cutaneous side effects (atrophy, telangiectasia, acne, dryness and rebound hyperpigmentation). Topical treatment takes long time ,after treatment with Kligman's formula for 6 months about 30% had completed clearing, 30% improved more than 50% and 30% did not response or developed rebound melasma. Newer drugs had recently been introduced e.g 4-butyl resorcinol, inhibit both tyrosinase and DHICA-oxidase (which is an alternative pathway enzyme for melanin synthesis) has been found to be as effective as hydroquinone without its side effects. Fullerine and Ascorbyl phosphate palmitate sodium is another recently introduce combination drugs with both antioxidation and whitening results without the side effect. To enhance delivering of drugs into the skin many treatment modalities had been introduce for delivering of ascorbic acid and tranxemic acid for whitening affects e.g. Iontophoresis and electroporation, and intradermal injection of tranxemic acid.

Many new combination drugs with medications that interfere with melanin biosynthesis pathway e.g. tyrosinase inhibitors (e.g. alpha-Arbutin) + exfoliating agents (e.g. glycolic acid) + transfer of melanins blocking (e.g. niacinamide) has recently been available. This product often resulted in mild to moderate whitening effect but is safe for long term use.

Laser Treatment

Ablative laser resurfacing and dermabrasion had been studied in treatment of melasma. Not only the procedures were painful and complicated, the healing and recovering took long times. Dyschromia (hyper and hypopigmentation) was common after the treatments. In Asians, scar a keloids were other important side effects. To be effective, the ablation depth should be enough to remove the follicular germ cells which locate as deep as mid dermis. This may explain why, dermabrasion had been claimed to be more effective than ablative laser resurfacing (CO₂ or Erbium YAG laser).The prolonged post treatment downtime and risk of hypopigmentation had discouraged performing this treatment for melisma [16-18].

For pigment selective lasers according to the principle of Selective Photothermolysis e.g. 532 nm frequency-doubled Q-switched Nd: YAG (2-3 J/cm²), 694 nm Q-Switched ruby (6-8 J/cm²) or 755 nm Q-switched alexandrite laser (6-9 J/cm²), the results was disappointingly. Diffusely located melanins in epidermis resulted in almost total epidermal necrosis after these lasers exposure. Epidermis sloughed off resulting in peeling similar to ablative laser resurfacing. Usually the deeply located follicular melanocytes persisted and repopulated the treated area resulting in rapid rebound hyperpigmentation. Injuries to basement membranes also produce melanin dropping, follow by melanophages. One month after treatment all treated area will be darker from both epidermal melanocytes hyperactivity and present of melanophages in the dermis. This condition was difficult to treat and hyperpigmentation post selective laser treatment of melasma will persist for years. Too aggressive selective pigment laser treatment with higher energy would end up destroying all melanocytes down to the depth of follicles end up with permanent hypopigmentation.

Intense pulsed light (IPL) with broad band light 535-1000 nm, initially had been claimed to be effective for hyperpigmented lesions. In Asians, it was later found out to be only minimally effective for

melasma. In Asians with SPT IV-VI, high energy fluence often resulted in epidermal burn followed by healing; hypopigmentation or post inflammatory hyperpigmentation .Lower energy fluence was not enough to reduce follicular melanocytes. Only patients with SPT II or III with focal epidermal hyperpigmentation e.g. solar lentigines had mild to moderate reduction in hyperpigmentation of lesions after multiple IPL treatment [19-21].

Minimal Photothermolysis Laser for Melasma

For the past five years, the author has studied the new technique using principle of minimal selective photothermolysis with 1064 nm Q-switched NdYAG laser, hat-top beam, 6-8 mm diameter spot size, 2-3.5 Joules/cm², 10 Hertz , accumulative energy for each spot was 10-70 Joules/cm² for treatment of melisma. Most of the patients were treated with Medlite C6 laser (cynosure-Conbio, CA, USA).

The author has found that more than 60% of the patients had good (>50% clearing, 30% had completed clearing) result after 10-20 weekly treatments. The complications were mild and transients including, pain, erythema, rash, urticaria and exacerbation of acne. Less than 10% had rebound melasma, recurrence of melasma was found in 30%. Hypopigmentation was found in 5%.

The important contributing factors for the good result of treatment are:

1. High cumulative energy of hat-top 1064 nm Q-switched Nd:YAG laser beam (10-20 passes)
2. Large diameter spot size (6-8 mm)
3. Rapidly repeated pulses (10 Hz)
4. Epidermal cooling with cool air (5°C)
5. Repeated treatment at 1-2 weeks interval
6. Long term photoprotection and topical whitening treatment

Eventhough the actual mechanism of treatment is still under study, minimal photothermolysis reaction by repetitive low threshold pulses resulted in melanins fragmentation, dispersion and eventually destruction of melanocytes. Clinically gradual depigmentation of melasma was observed. Topical moderate potency whitening agents e.g. alph-Arbutin, Fullerine + Ascorbyl phosphate palmitate sodium together with UVA + UVB blocker sunscreen prevented recurrence.

Treatment Technique

The treatment is done by delivering high repetitive(10 Hz) 5 nanoSecond, 1064 nm laser ,homogenous spot size pulses with sub-immediate whitening threshold fluence (usually 2 to 3.5 Joules/cm²) on to the lesions until immediate erythema is seen. Pulses of laser should be applied perpendicular to the surface with 10-20% overlapping between pulses and move laser pulses slowly across the lesions. Usually approximate 20 passes are performed on each spot. If the melanins are mainly in the epidermis, there will be immediate lightening of color of lesions. Patients will feel stinging sensation and warm. Cool air (5-10°C) is applied just before and after the treatment to reduce discomfort. Erythema will last a few hours.

The treatment should be done at short interval of 7-14 days before new epidermal cells with melanin granules replace the treated layer. Usually after about 10 treatments epidermal melasma will fade between 50- 80%. Dermal melanophages will also response to this treatments but take longer time and and higher repetition.

To continue repeated treatments more than 10 times have to be judged case by case. The incidence of side effects especially hypopigmentation related to number of treatments. Detection of mottling hypopigmentation indicates that the treatment may reach the stage of permanently destruction of melanocytes which is undesirable. The treatment if needed to be done should be performed only to the remaining hyperpigment areas. The author has found that for melasma with melanophages the improvement was not as dramatic as epidermal lesion alone. The migration of melanophages needs longer time.

Topical whitening drugs and UVA and UVB blockers (SPF >30 and PA +++) are prescribed after the first treatment and continued for at least six months. The choice of whitening agents has to be judged case by case. The case that has been using hydroquinone containing cream for some time should continue with the treatment and slowly replace by other safer medications. Immediate termination of hydroquinone often results in rapid rebound hyperpigmentation. Cases without history of hydroquinone should use other newer agents with less long term side effects e.g. Alpha Arbutin, Fullerine etc.

Dermal melanocytic lesions e.g. acquired bilateral nevus of Ota like macules (Hori's nevus) and brownish lesion of Nevus of Ota also fade after repeated (more than 10) treatments. Blue or black nevus of Ota lesions usually does not response, repeated high energy (>8 Joules/cm²) is still the recommend treatment. Periorbital darkening also improved after 10 treatments.

Post Inflammatory Hyperpigmentation (PIH) is another condition which response rapidly to this new treatment. PIH or hyperpigmentation after skin injuries from any treatments is the result of both epidermal melanin synthesis and melanohages. It will response after few treatments. Melanins fragmentation /dispersion and enhancing of melanophages migration may explain this rapid response. In this condition, usually the numbers of melanocytes were reduced but they contained large clumps of melanin. These cells will be very sensitive to exposure with 1064nm laser light. Lower fluence is recommended for dark lesion. Immediate grayish white discolouration is a warning that too high energy has been delivered. Energy fluence should be lowered.

For epidermal lesions with hyperplasia of melanocytes e.g. solar lentigoes, ephilides, lentigines and café au lait macules usually response faster with 532 nm, Q-switched Nd:YAG laser treatments. For the collimated beam, lower energy fluence should be applied. This may reduce the risk of basement membrane injuries and PIH. The author has now used immediate grayish discolouration as the treatment end points. There will be thin brownish scabs for 3-5 days. After the scab fell off, faint hypopigmentation persisted for few weeks but PIH was much lower than using the old parameter.

The author has treated more than 500 cases of melasma with Minimal Photothermolysis Technique. In epidermal melasma more than 80% reduction of pigmentation at lesions was obtained in more than 70% of cases, the remaining 30% has 50-80% response after 10 weekly treatments. 50% of combined melasma has 50-70% response. PIH or axillar hyperpigmentation responded better and faster. All cases received broad spectrum sunscreen (Anthelios XL, La Roche Posay, France, SPF 50, PA+++), with topical bleaching creams 7% Arbutin solution, triple drugs or Kligmen's formula (Trilumar, Galderma) applied twice daily. Few cases with very dark dermal lesions receive weekly intradermal transamin (5 mg/ml) for 3-4 times.

A case with history of previous topical hydroquinone treatment was maintained with topical triple drugs (Trilumar). Long term follow up

of more than 5 years after treatment was done in 30 cases. More than 30 % still had good result (50-75% reduction of MASI scores). Recurrence occurred in 30% of cases and confetti like hypopigmentation developed in 5% of cases [22-24] (Figures 1-3).



Figure 1: Pre and post 10th Medlite C6 treatment of epidermal melasma, 1064 nm, 3.4 J/cm², 6 mm spot size, 10 Hz, 20 passes with cool air cooling at weekly interval. There is more than 80% clearing of lesions with much improvement in skin textures. (Clin Prof Niwat Polnikorn, Bangkok, Thailand)



Figure 2: Pre and post 10th of dermal melasma and PIH with Medlite C6, 1064 nm, 3.4 J/cm², 6 mm spot size, 10 Hz, 20 passes, weekly interval. There was more than 50% reduction of dermal melasma and PIH. (Clin Prof Niwat Polnikorn, Bangkok, Thailand)



Figure 3: Pre and post 8th treatment of combined epidermal melasma and Acquired Bilateral Nevus of Ota like Macules (Hori's nevus) with Medlite C6, 1064 nm, 3.4 J/cm², 6 mm spot size, 10 Hz, 20 passes. There was more than 80% clearing of epidermal melasma and 50% lightening of Hori's nevus. (Clin Prof Niwat Polnikorn, Bangkok)

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