Lasers in Melasma: A Review with Consensus Recommendations by Indian Pigmentary Expert Group

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Abstract
Lasers have come up as the newest therapeutic modality in dermatological conditions including melasma. In this article, as a group of experts from Pigmentary Disorders Society in collaboration with South Asian Pigmentary Disorders Forum (SPF), we have tried to discuss the lasers which have been used in melasma and formulate simple consensus guidelines. Following thorough literature search, we have summarised the rationale of using the lasers and the supporting evidences have also been provided. It is clear that laser cannot be the first line treatment for melasma. However, it can be used as an adjuvant therapy in resistant cases, provided the selection of patient and counselling has been done properly.

Key Words: Lasers, melasma, expert opinion, consensus

Introduction
Melasma is a common acquired facial pigmentary disorder and challenging to treat. Triple combination (FTC) creams and sunscreens remain the cornerstone of therapy followed by maintenance with hydroquinone (HQ) and non-HQ skin-lightening agents. Peels have made successful inroads and are used frequently as an adjunct to medical management.

A variety of lasers and light devices have been used with varying degrees of success in melasma. The vast array of devices and combination protocols that have been tried in melasma clearly indicate that no single modality is singularly effective. Q-switched lasers (QSL), fractional lasers, ablative lasers, intense pulsed lights (IPLs), copper bromide laser, thulium laser, and their combinations have all been used, but response is unpredictable, and the pigmentation frequently recurs. Since melanin has a broad absorption spectrum (630-1100 nm), a variety of lasers and light sources can be used, but the selection of patient, counselling and post-procedural follow-up form the backbone of laser therapy.

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Disorders Society (PDS) in a collaborative discussion called South Asian Pigmentary Forum (SPF).

The lasers and light-based devices used in melasma include:
- IPL\(^{[1]}\)
- Fractional lasers - Fractional nonablative lasers and fractional ablative lasers\(^{[2]}\)
  - 1540 nm/1550 nm Er:Glass laser
  - 2940 nm Er:YAG laser
  - 10,600 nm CO2 laser
- Ablative lasers\(^{[3]}\)
- Fractional lasers with transdermal drug delivery
- QSLs-QS 1064 nm, QS 585/595 nm laser
- Fractional QS:YAG laser and fractional QS ruby 694 nm lasers
- Picosecond lasers
- Sublative lasers - fractional 1927 nm, thulium fiber laser
- Other lasers - copper bromide laser
- Combination techniques.
  - Ablative CO2 + QS alexandrite 755 nm laser\(^{[4,5]}\)
  - IPL + QS 1064 nm laser toning
  - Low-fluence QS 1064 nm + QS 585 nm gold toning
  - Low-fluence QS 1064 nm QS YAG + 1550 nm fractional laser
  - Fractional 2940 nm Er:YAG + QS:YAG.

Laser toning has gained immense popularity in Southeast Asia. The concept of laser toning (low fluence, multipass technique, multiple sessions at weekly intervals) is based on the proposed novel theory of subcellular selective photothermolysis, proposed by Mun \textit{et al.} in 2011.\(^{[6]}\) They studied the ultrastructural changes within melanosome, using transmission electron microscopy. They found a reduction in the dendrites of epidermal melanocyte, following laser treatment. Laser treatment caused selective photothermolysis on Stage IV melanosome, wherein the melanocytes remained intact and only the melanosomes were destroyed. They concluded that laser toning was an effective method for treating melasma through subcellular-selective photothermolysis.

Traditional treatments were based on the principle of selective photothermolysis which results in destruction and death of pigment-containing cells. In response to cell death, inflammation follows and results in repigmentation and recurrence or in postinflammatory hyperpigmentation (PIH). The adverse effects were attributed to laser-induced basal layer damage and dermal inflammation leading to recurrence of melasma on sun exposure, PIH, rebound hyperpigmentation, and mottled depigmentation. This is in contrast to the principle of subcellular selective photothermolysis, which uses high-peak power, ultrashort pulse duration [5ns], and flat-top beam resulting in destruction of only melanin in the target cell but leaving the cell alive. Since fluence used is very less and there is no cell death, inflammation and heating is minimum, thus reducing the chances of recurrence.

**Rationale for Use of Lasers in Melasma**

Melanin has a broad absorption spectrum (630–1100 nm) allowing a variety of lasers and light sources to be used. Melanosomes have a short thermal relaxation time (50–500 nanoseconds). Longer wavelengths penetrate deeper to target the dermal pigment, but melanin absorption is better with shorter wavelengths.

QS Nd:YAG laser [(QS:YAG) 1064 nm] has a pulse duration of 10 ns. Hence, the QS:YAG laser seems like a logical choice for some cases of melasma, especially in individuals with darker skin tones.

**Q-switched Nd:YAG Laser**

Low-fluence Q-switched (LFQS) Nd:YAG laser is the most widely studied laser for the treatment of melasma. However, there are no randomized controlled trials (RCTs) comparing the effectiveness, safety, and tolerability of Q-switched Nd:YAG laser (532 nm) versus topical corticosteroids or hydroquinone.

We have considered 10 studies [Table 1] which evaluated the role of LFQS Nd:YAG laser on 446 patients of melasma.\(^{[7,10]}\)

Out of these 10 studies, 6 were RCTs, 3 were nonrandomized uncontrolled studies, and 1 of them was a simple case–control study. Ninety-two patients were evaluated in the three uncontrolled studies and the authors concluded that LFQS Nd:YAG laser monotherapy had good results in melasma.\(^{[7,9]}\)

However, the drawback of these studies was the small sample size, which puts a question mark on the effectiveness of LFQS Nd:YAG laser monotherapy in melasma. The effectiveness of Nd:YAG laser was found to be inferior to low-power fractional CO2 laser\(^{[11]}\) and equal to that of LFQS alexandrite laser (755 nm).

To note, Chan \textit{et al.} reported a series of facial depigmentation with the use of low-fluence QS:YAG laser. They concluded that laser toning with LFQS 1,064 nm Nd:YAG laser for skin rejuvenation and melasma can be associated with mottled depigmentation. Hence, caution needs to be exercised while performing this procedure and the risks need to be explained to patients.\(^{[17]}\)

The results of LFQS Nd:YAG laser (1,064 nm) were found to be better when combined with IPL. However, number of patients was less and follow-up period was small.\(^{[13]}\)

In addition, Na \textit{et al.} observed that combination treatment may provide more rapid clinical resolution in mixed-type melasma with possible long-term clinical benefits.\(^{[10]}\)

Besides, LFQS when combined with long-pulse Nd:YAG has shown better results in terms of reduction in melasma area.
Table 1: Summary of a few important studies conducted on the safety and effectiveness of various lasers in melasma

| Study            | Conclusion                                                                 | Level of evidence | Comment                                                                 |
|------------------|---------------------------------------------------------------------------|-------------------|------------------------------------------------------------------------|
| Kim *et. al.*    | LFQS Nd:YAG laser showed good results                                       | III               | LFQS Nd:YAG laser is not recommended as monotherapy. However, it can be combined with other lasers, peels, and oral adjuvants |
| Hofbauer *et. al.* | LFQS Nd:YAG laser was superior to 25% TCA peel                            | II                |                                                                        |
| Sim *et. al.*    | LFQS Nd:YAG laser was inferior to low-power fractional CO₂ laser          | II                |                                                                        |
| Moubasher *et. al.* | LFQS Nd:YAG laser was equally effective as LFQS alexandrite laser        | II                |                                                                        |
| Jalaly *et. al.* | LFQS Nd:YAG laser in combination with IPL was superior to IPL alone     | IV                |                                                                        |
| Alsaaad *et. al.* | LFQS Nd:YAG laser of pulse durations 5 ns and 50 ns was equivocal       | II                |                                                                        |
| Choi *et. al.*   | LFQS Nd:YAG laser in combination with long-pulsed Nd:YAG was superior to LFQS Nd:YAG laser alone | IV                |                                                                        |
| Shin *et. al.*   | Efficacy of LFQS Nd:YAG laser is increased when combined with oral TXA   | II                |                                                                        |
| Vachiramon *et. al.* | Efficacy of LFQS Nd:YAG laser is increased when combined with glycolic acid peel | II                |                                                                        |
| Lee *et. al.*    | Efficacy of LFQS Nd:YAG laser is increased when combined with Vitamin C   | III               |                                                                        |
| Zhou *et. al.*   | QSRL with sonophoresis on levorotatory Vitamin C showed good results     | III               | QSRL cannot be recommended until further studies are conducted, due to possibility of postinflammatory hyperpigmentation |
| Kopera *et. al.* | QSRL showed moderate results, but side effects were alarming             | II–III            | Given the risk of postoperative dyspigmentation, the authors concluded that it was not safe enough to recommend for routine use for melasma in Southeast Asian population |
| Taylor *et. al.* |                                                                           |                   |                                                                        |
| Tse *et. al.*    |                                                                           |                   |                                                                        |
| Fabi *et. al.*   | LFQS Nd:YAG laser was better than alexandrite laser                       | II                | Alexandrite laser cannot be recommended until further studies are conducted |
| Jalaly *et. al.* | Low-power fractional CO₂ laser showed good results                        | II                | Since the study was conducted in non-Asian population and the follow-up was short, fractional CO₂ laser cannot be recommended |
| Attwa *et. al.*  | Er-YAG laser showed good results                                          | III               | Postinflammatory hyperpigmentation was a significant adverse effect, and thus, this laser cannot be recommended |
| Manaloto *et. al.* | Er-YAG laser resurfacing improved melasma                                | II–III            | Postinflammatory hyperpigmentation outweighs any benefit. Can be recommended for refractory cases only |
| Brauer *et. al.* | Fractional 1550/1540 nm nonablative laser shows promising results        | II–III            | Use of low fluence, variable pulses, and pretreating all patients with hydroquinone for 6 weeks before laser therapy is recommended |

LFQS: Low-fluence Q-switched, QSRL: Q-switched ruby laser, IPL: Intense pulsed light, TXA: Tranexamic acid

severity index (MAI) score and significantly less adverse effects, when compared with LFQS Nd:YAG laser alone.16

Tian *et al.* reported a novel technique using a combination of fractional 2940-nm Er:YAG and 1064-nm Q-switched Nd:YAG lasers. Authors reported a rapid improvement in two cases, within a month of treatment. The novel strategy was found to deliver a safe, tolerable, and sustained result within a short period of treatment.19

Efficacy of LFQS Nd:YAG laser is increased when combined with oral tranexamic acid, glycolic acid peel, Vitamin C, etc.20–22

Q-switched Ruby Laser

We did not find any study which has evaluated the role of Q-switched ruby laser (QSRL) as a monotherapy in the treatment of melasma. Zhou *et al.* published
a study which was conducted on Chinese patients, on the role of 694-nm fractional Q-switched ruby laser (fluence 2.5–3.5 J/cm², 7.1 × 7.1 mm spot size, 27.7% area coverage) in combination with sonophoresis on levorotatory Vitamin C. There was a reduction in MASI score by 35% at the end of the study. However, there are no further studies to validate the results in Indian population. Besides, previous studies have reported the development of PIH and recurrence of melasma following the use of ruby lasers. Hence, it is not safe to use QSRL routinely in Southeast Asian population.

**Intense Pulsed Light**

IPL, a nonlaser light source that emits light with wavelengths between 515 and 1200 nm, has been studied alone and in comparison with hydroquinone for the treatment of melasma. IPL appears to give modest improvement as an adjunctive therapy in patients with melasma refractory to topical therapy alone and may be useful in patients who do not mind the 1- to 2-week recovery time.

**Alexandrite Laser**

Fabi et al. reported a randomized split-face clinical trial, comparing the effectiveness of alexandrite laser and LFOS Nd:YAG laser. The latter was found to be better, though statistically insignificant.

**Fractional and Ablative Lasers (CO₂ Laser)**

These are not used as monotherapies on account of the high incidence of side effects. However, low-fluence lasers are being used. Jalali et al. conducted a split-face double-blinded randomized trial and compared low-power fractional CO₂ laser with LFQS 1,064 nm Nd:YAG laser. Fractional CO₂ laser showed good results in terms of reduction in melanin index and MASI score. However, it is not wisely to recommend the use of this laser in Indian population due to financial constraints, short follow-up period, and the fact which cannot be overlooked is that the study was conducted in non-Asian population.

**Er-YAG Laser**

Attwa et al. conducted an uncontrolled study on the effectiveness of Er-YAG laser and reported significant improvement in MASI score. However, PIH was a statistically significant side effect.

Besides, Manaloto et al. concluded that Er-YAG laser can be recommended for refractory cases only.

**Er-Glass Laser**

Tourlaki et al. conducted a nonrandomized study on Er-glass laser. The reduction in MASI score was significant at the end of 1 month, but this was not sustained.

**Vascular Laser**

Angiogenic melasma has been shown to respond to vascular lasers, which act by targeting vascular endothelial growth factors and the blood vessels of dermis.

**Copper Bromide Laser**

Copper bromide laser produces 2 wavelengths – 511 nm green light to treat pigmentary lesions and 578 nm yellow light to treat vascular lesions. Both wavelengths can be used simultaneously to treat melasma, every 2 weeks for 8 weeks. It may target vascular component as well as pigmentation in melasma.

Eimpunth et al. conducted a nonrandomized study in Thailand. They used copper bromide laser (dual-wavelength, 511 and 578 nm, fluence 7–19 J/cm²) but could not find any statistically significant improvement.

In another split-face RCT conducted by Hammami et al., copper bromide laser was not found to be better than triple combination creams.

**Thulium Fiber Laser**

Thulium fiber laser (1927 nm) nonablative laser has also shown promise in the management of melasma. Treatments are performed once a month for 3–4 months. It is a fractionated laser that produces small amount of epidermal ablation and greater amount of dermal heating.

**Fractional Nonablative Lasers**

Fractional 1550/1540 nm nonablative laser therapy is the only laser treatment for melasma that has been approved by the FDA, and it has shown promising results. Given the risk for hyperpigmentation, some authors suggest using lower fluences, variable pulses, and pretreating all patients with hydroquinone for up to 6 weeks before laser therapy, especially in patients with a history of PIH.

Brauer et al. studied a low energy, low density, nonablative fractional 1927 nm laser for melasma, PIH, and photodamage. In this study, favorable outcomes were demonstrated and results were maintained at the 3-month follow-up.

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**Conflicts of interest**

There are no conflicts of interest.
What is new?
- Lasers can be used in selected patients with resistant melasma after thorough counseling and preferably after conducting test treatments.
- Low-fluence Q-switched (LFQS) Nd-YAG laser seems to be the best option for refractory cases of melasma, especially in individuals with darker skin tones. However, it is not recommended as monotherapy. It can be combined with other lasers, peels, and oral adjuvants.
- Q-switched ruby laser and Erbium YAG laser are better avoided, due to the risk of developing post-inflammatory hyperpigmentation.
- Fractional 1550/1540 nm non-ablative laser therapy is the only laser that has been approved by the FDA for melasma. To minimise the chances of post-inflammatory hyperpigmentation, it is advisable to use lower fluencies, variable pulses and pre-treatment with hydroquinone for 4-6 weeks before laser therapy.

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