Laser Toning in Melasma

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Abstract

Melasma is a common acquired disorder of hyperpigmentation. A variety of treatment options has been suggested for the management of melasma. A range of different lasers had been tried in the treatment of melasma. Q-switched Nd-YAG laser (QSL) is the most commonly used laser in the treatment of melasma. Recently, laser toning or low-fluence, multi-pass technique has become popular in treatment of melasma. Authors aimed to review the procedure, its effectiveness, combination therapies using laser toning, and complications of laser toning. A PubMed search was made using keywords such as laser toning, QSL, melasma, and lasers in melasma, and relevant articles were reviewed.

Keywords: Laser toning, melasma, Q-switched Nd:YAG laser

Key Messages: Laser toning is a safe and effective treatment in the management of melasma. Combination therapies including laser toning and topicals often produce satisfactory responses. It is considered as a third-line option in the management of melasma in those patients who failed to respond adequately to trial of medicines and peels. A careful watch should be kept on side effects such as mottled hypopigmentation.

Introduction

Melasma is a common acquired disorder of hyperpigmentation characterized by symmetrical hyperpigmentation, appearing as light brown to dark brown patches typically on malar areas, forehead, and chin. Although it is just a benign hyperpigmentary condition, it can adversely affect the patient's self-esteem and quality of life.[1] The prevalence of melasma varies with the ethnicity of the population[2] and contribute to 4%–10% of new cases in dermatological clinics.[3] It affects females more than males.[4] The etiopathogenesis of melasma is unclear and multifactorial with genetic and environmental factors playing their role.[5] The most important risk factors for melasma are Fitzpatrick skin type III and above, ultraviolet (UV) light exposure, pregnancy, exogenous hormones, drugs, and thyroid dysfunction.[5]

Because of unclear etiopathogenesis and recurrent and relapsing nature of the disease, the treatment of melasma is difficult and frustrating for the treating physician and the patient.

A variety of treatment options has been suggested for the management of melasma. These include topical medications (such as hydroquinone, azelaic acid, arbutin, kojic acid, tranexamic acid), chemical peels, oral medications (antioxidants, tranexamic acid), lasers, and lights.[6] An Indian pigmentary expert group proposed a treatment algorithm for melasma.[7] They proposed various topicals and sunscreens as the first-line treatment, chemical peels as a second-line treatment, and lasers and light as a third-line therapy. The lasers and light treatment were reserved for patients with refractory melasma who failed to respond to topicals and chemical peels.[7]

Melasma can be of epidermal, dermal, or most commonly of mixed type. Topicals and peels often produce a satisfactory response in epidermal melasma but are partially effective in dermal or mixed melasma. These patients often require lasers for the treatment.

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A range of different lasers had been tried in the treatment of melasma including full-face resurfacing using CO_2 or erbium YAG laser, a variety of fractional ablative and non-ablative lasers, intense pulsed light (IPL), and q-switched Nd-YAG laser (QSL).[8]

QSL at 1064 nm is the most commonly used laser in the treatment of melasma because of its deeper penetrating properties and safety in pigmented skin. However, earlier reports of treatment of melasma using QSL were not encouraging,[9,10] and many articles reported complications such as relapse,[11] exacerbation of melasma, or hypopigmentation.[12]

Goldberg and Metzler[13] in the year 1999 proposed the concept of laser toning. They used multiple passes of low-fluence QSL to improve photoaged skin. Kim *et al.*[14] used the same technique in zebrafish skin to selective destroy the melanosomes without the cell death. This opened up a new and safe modality of the treatment of melasma. Since then, many reports were published especially from Asia, which proves its safety and efficacy.

Laser Toning

Laser toning or low-fluence, multi-pass technique is a popular method for treatment of refractory melasma. The term "laser toning" originates from the improvements in skin tone that result from the use of the laser.[15]

The procedure

The procedure of laser toning is relatively simple:

- Choose 1064-nm wavelength of QSL.
- The largest spot, 6–10 mm available on the system, should be chosen.
- The fluence chosen will be in between 0.8 and 2 J/cm^2 depending on the spot size of the laser. The starting fluence is chosen according to the spot size available with system and color of melasma. For a spot size of 8–10 mm, the fluence range should be between 0.8 and 1.4 J/cm^2.
- The handpiece should always be held perpendicular to the skin.
- Frequency should be 5–10 Hz.
- There should not be an overlap of more than 10%–15% between the two pulses.
- The endpoint of the treatment will be faint erythema or three to four passes (if there is no perceptible erythema).
- The darker the melasma, lesser will be fluence and vice versa.
- A minimum of 10–12 sessions with a weekly interval or once in 15 days should be conducted. The authors use it once in 15 days because we have found that once-a-week treatment increases the chances of mottled hypopigmentation in Indian skin.
- After procedure, broad-spectrum sunscreen is used. Patients can resume their topical after 1–2 days after procedures.

Mechanism of action

Treatment of melasma with laser is always a controversial issue. The traditional QSL treatment is based on the principle of selective photothermolysis, which uses a high fluence to destroy the pigment-containing cell. Because of cell death, there will be release of prostaglandins and cytokines, which results in inflammatory state and damage to basement membrane,[11] resulting in relapse, exacerbation of melasma, or pigmentary changes.

The collimated flattop beam, large spot size, ultrashort pulse duration, low-fluence, and multiple passes of QSL are believed to cause minimal damage to the melanocytes, but it can destroy the melanosomes and melanin granules within melanocytes and keratinocytes but keeping the cell membrane and nucleus intact, thus avoiding cell death. This mechanism is known as "subcellular selective photothermolysis."[14] The long dendritic processes of hyperactive melanocytes are cutoff (dendrectomy), and there is functional downregulation of melanocytes, which results in the production of a reduced number of melanosomes.[15]

As there is no cell death and heating of skin is kept to a minimum, there are fewer chances of exacerbation of melasma.

Melasma can be an epidermal, dermal, or more often of mixed type. Using large spot size and longer wavelength, the depth of penetration can be increased even with less fluence. This helps in targeting the deeper component of melasma and melanophages in dermis. It is mandatory to use a system with top-hat fluence for laser toning. The top-hat beam distributes the fluence all along the spot and thus avoids the hot spot as in Gaussian beam lasers. Laser toning uses low-fluence and multi-pass technique as against the single-pass high fluence treatment of selective photothermolysis. Using the multiple passes, the melanosomes are heated slowly and destroyed, but the cell membrane and nucleus of the cell are kept intact and thus the cell death is avoided.

Various studies confirmed these findings. Kim *et al.* studied histopathology of eight Korean women treated with laser toning. They reported that the treated skin showed a decrease in the number of melanosomes and reduced expression of melanogenesis-associated proteins with a normal number of melanocytes.[15] They postulated that the decreased function of melanocytes occurs via the downregulation of melanogenesis, tyrosinase, TRP-1, and TRP-2. Melanogenic stimulators, including a-MSH and NGF, were also reduced. Similar results were also reported by Nam *et al.*[16] They also reported that there is a positive correlation between number of passes and pigmentation improvement. Omi *et al.*[17] compared ultrastructural changes after toning with QSL to q-switched ruby laser and concluded that QSL toning offered superior results

with less epidermal disruption and cellular damage, thus, confirming the safety of toning with QSL.

To study the pattern of relapse after discontinuation of laser toning, Kim *et al.*[18] studied the recovery of pigmentation after laser toning in adult zebrafish skin. They found that melanosomes may regenerate within melanocytes if melanocytes are not destroyed. If tyrosinase inhibitors are combined with laser toning, they prevent the relapse of melasma till the patient is on the drugs, thus creating an opportunity to maintain remission. Arbutin and Kojic acids that are commercially available tyrosinase inhibitors do not completely shutdown melanin regeneration.[18]

Review of literature

Laser toning is found to be effective in the treatment of melasma. It can effectively reduce the size, homogeneity, and pigmentation of melasma lesions. Various studies in the past few years confirmed these findings [Table 1].

Polnikorn[19] successfully treated two cases of refractory melasma with laser toning. He combined it with 7% arbutin cream to prevent recurrence. Suh *et al*.[22] in their study using 1064-nm QSL at the 1-week interval for 10 weeks showed that it is a safe and effective modality for treating melasma in Asian patients.

Sim *et al.*[23] used laser toning to treat melasma in 50 Asian patients with 15 weekly treatments. They reported good improvement on average with an improvement rate of 50%–74%.[23] Kim *et al.*[25] studied 22 Korean women with laser toning with a total of 5 sessions of low-fluence pulse to pulse (PTP) mode Nd:YAG laser treatment at 2-week interval. They reported significant improvement in 60% of their patients with a reduction in melasam area severity index (MASI) score by 20% and lightness measured by colorimeter was significantly increased by 1.3 points.[25]

Tian[24] studied the effect of laser toning in 38,970 cases. He reported 21,940 patients (56.3%) reported fair improvement; 8,690 (22.3%) had good improvement; and 1,987 (5.1%) had excellent improvement. A total of 3,273 (8.4%) patients had noticeable improvement, whereas 3,080 (7.9%) had little or no improvement.[24]

Gokalp *et al.*[26] studied 34 patients and reported 58.8% patients to have at least a 50% improvement in melasma severity with the mean modified melasma area severity index (mMASI) score decreased from 6.7 to 3.2. However, when these patients were followed up for 1 year, recurrence was observed in 20 patients (58.8%) and the mean mMASI score increased from 3.2 to 5.8 in all patients.[26]

Kaminaka *et al.*[27] studied laser toning in 22 patients and reported a 50% reduction in melanin index after a series of weekly 10 sessions. They also reported a recurrence rate of 16.7% in their study.[27]

In a recent study, Choi *et al.*[28] reported 20 patients treated with 10 weekly sessions of toning. They reported good to fair improvement in 70% of their patients with two developing mottled hypopigmentation and hyperpigmentation.[28]

Combination Therapy

Laser toning can be combined with various other topical or physical treatment modalities to obtain better efficacy and to increase the safety of treatment by minimizing complications. Topical therapy with hydroquinone is the cornerstone of treatment of melasma. Wattanakrai *et al.*[29] treated 22 patients with melasma in a split-face trial. They compared the combined treatment of laser toning and 2% hydroquinone with 2% hydroquinone alone. After five weekly treatments, the combination worked better.[29]

Jeong *et al.*[30] studied a combination of topical triple combination (TC) with laser toning. They treated 13 patients with topical treatment with TC cream or 1064-nm QSL treatment on opposite sides of the face for 8 weeks, and then treatments were reversed for 8 weeks and concluded that treatment after topical TC cream was found to be safer and more effective than the posttreatment use of topical agents.[30]

Bansal *et al.*[31] compared efficacy of toning with topical 20% azelaic acid cream and their combination in melasma in 3 study groups of 20 patients each. They concluded that the combination of toning and topical 20% azelaic acid cream yields better results as compared to low-fluence QSNYL and azelaic acid alone.[31]

Chemical peeling is a popular method of treatment in the management of melasma. Saleh *et al.* compared laser toning alone or in combination with modified Jessner peel in 19 patients. They treated one side of the face with laser toning and alternating laser and modified Jessner peel on another side. They found that both methods were equally effective; however, the incidence of mottled hypopigmentation is significantly less in the side treated with a combination and skin texture, brightness, and color homogeneity were improved more commonly with combination therapy.[32]

Vachiramon *et al.*[33] studied the combination of laser toning alone and in a combination of 30% glycolic acid peels in 15 male patients in a split-face study. They reported temporary improvement in both sides but the side effects such as post-inflammatory hyperpigmentation or even depigmentation (in one case) were more common in the side treated with combination protocol.[33]

Kauvar[34] demonstrated good efficacy using a combination of microdermabrasion and low-fluence QS Nd: YAG laser, applying topical lighteners between laser sessions.[34]

Ustuner *et al.*[35] studied 16 patients of refractory melasma with laser toning against laser toning plus microneedling and topical vitamin C in a split-face study. They reported significant improvement of combination-treated side than the laser-treated side. In another split-face study

Table 1: Studies demonstrating efficacy of laser toning in melasma

Author	Number of patients	Parameters used					Efficacy	Complications
		Number of sessions	Spot (mm)	Fluence (J/cm²)	Passes	Interval		
Polnikorn[19]	2	10	6	3.4	20	Weekly	Good improvement without recurrence	None
Jeong *et al.*[20]	17	8	7	2–2.5	3–10 until erythema	Weekly	Split-face study. 10 (58.8%) showed good improvement (50%–75%)	Two have partial recurrence at 2 months
Cho *et al.*[21]	25	Mean 7 (5–15)	6 4	2.5 for whole face 4–5 on lesions	2 2	2 weeks	Eighteen of 25 patients were very satisfied or satisfied, 5 were slightly satisfied, and 2 were unsatisfied	Two patients developed hypopigmentation
Suh *et al.*[22]	23	10	4–6–8	2–4	Not mentioned	Weekly	Significant improvement in all patients	Prolonged erythema in three patients, PIH in three, and hypopigmentation in three
Sim *et al.*[23]	50	15	8	2.8	Mild erythema	Weekly	Improvement rate of 50%–74%	None
Tian[24]	38,970	12	8	2	2–3	Weekly	21,940 patients (56.3%):fair improvement. 8,690 (22.3%): good improvement. 1,987 (5.1%):excellent improvement. 3,273 (8.4%):noticeable improvement, 3,080 (7.9%):little or no improvement	None
Kim *et al.*[25]	22	5	7	2.5 (PTP mode)	5–7	2 weeks	60% significantly improved. MASI reduced by 20% and lightness index increase by scale of 1.3 points	Erythema, dryness, pain, and itching
Gokalp *et al.*[26]	34	6–10	6	2.5	Multiple	2 weeks	20 of 34 patients (58.8%) had more than 50% improvement	Recurrence of melasma in 20 patients (58.8%) at the end of 1 year
Kaminaka *et al.*[27]	22	10	6	2–2.5	3	Weekly	Split-face study. Treated side has 50% reduction in melasma	Recurrence rate was 16.7%
Choi *et al.*[28]	40	10	8	1.2–2	Mild erythema	Weekly	2.5% (1 pt) excellent improvement, 35% (14) good, 37.5% (15) fair, 15% (6) poor, and 10% (4) no improvement	Two patients hypopigmentation and PIH

PIH = post inflammatory hyperpigmentation

of melasma by Lee *et al*.[36] conducted on eight patients, four sessions of the toning combined with the ultrasonic application of topical vitamin C resulted in a faster clinical response, more significant improvement, and higher patient satisfaction compared to laser monotherapy.

Interactions between the altered cutaneous vasculature and melanocytes have been implicated in the development of hyperpigmentation in melasma.[37] Human melanocyte shows functional VEGF receptor and hence they can respond to angiogenic factors.[38] Na *et al.*[39] reported that only the area affected by melasma presents a pronounced vascular change, showing significant increases in the number and size of dermal blood vessels. Moreover, they considered that the number of vessels is positively related to the degree of pigmentation.[39] Park *et al.*[40] demonstrated that the degree of erythema is positively correlated with that of pigmentation in a melasma lesion. Hence dermal vasculature can be a target for melasma treatment.

Kong *et al.*[41] combined pulsed dye laser (PDL) with laser toning in 17 patients with melasma. All patients received nine sessions of toning on both sides of the face and one side received three sessions of PDL along with toning. They found no difference in outcome on both sides with equal improvement in all but seven patients. These seven patients had widened capillaries on dermoscopy and responded better to the combination of PDL and toning.[41]

Choi *et al.*[42] combined quasi-long pulsed Nd:YAG and laser toning in very low fluences in the management of 30 patients with aggravated melasma because of previous treatment. They reported significant improvement in all patients with a mean reduction of MASI from 10.84 to 3.22. They postulated the quasi-long pulsed Nd:YAG melasma activity to prevent rebound hyperpigmentation via dermal remodeling and its effect on dermal vasculature.[42] They postulated 300-μs pulsed mode used in dual toning induces a good wound-healing response with release of heat shock proteins, reduction of proinflammatory interleukin 8, and induction of transforming growth factor b. This results in active collagenesis and remodeling and results in better clearance of melasma with improved skin tone.

Shin *et al.*[43] studied combination of oral tranexamic acid with laser toning in 48 patients. They found the results were superior with combination than in laser alone patient group.[43]

Toning can be combined with other light-based therapies. Kim *et al.*[44] did a split-face study in which QSL was combined with 1550-nm fractional erbium glass laser on one side and only QSL on another side. They found no difference in outcome on both sides.[44]

Cunha *et al.*[45] studied six patients of refractory melasma with the combination of IPL with toning at a monthly interval and reported significant improvement in all the patients. Similar results were also reported by Yun *et al.*[46] in 12 Korean patients treated with fractionated IPL and laser toning. They reported significant improvement in combination group than IPL alone group.[46]

Kwon *et al*.[47] studied the combination of fractional microneedling radiofrequency with laser toning to laser toning alone in a retrospective study. They treated 56 patients with 10 weekly sessions of combination or QSL alone. They reported not only the combination group improved better (68%–54%), but also the treatment-related side effects such as mottled hypopigmentation and rebound hyperpigmentation were less on combination-treated side.[47]

Complications

Safe and effective laser toning is not free from complications. Reported complications from laser toning include pain during the procedure, rebound of melasma, hyperpigmentation, guttate leukoderma, physical urticaria, acneiform eruption, minute petechiae, whitening of fine facial hair, and herpes simplex reactivation. Most of these complications are mild and self-limiting except hypo- or depigmentation.

Relapse and worsening of melasma have been reported after toning. The risk factors for relapse may be high cumulative fluence and small spot used for the treatment. Hofbauer Parra *et al.*[48] studied 20 Latin American patients with laser toning and reported significant improvement in all patients with minimal side effects. However, 81% of their patients relapsed or worsened after discontinuation of treatment.[48] The high relapse rate was also reported in other studies.[18,26,27]

Confetti-like hypopigmentation or punctate leukoderma is the most distressing complication of repeated low-fluence laser therapy. It can develop after several sessions or as early as the second session.[49] The cumulative dose of repetitive laser treatment may affect melanocyte function, resulting in the development of hypopigmentation.[50]

Various studies and case reports[29,49,51] reported a higher incidence of mottled hypopigmentation in patients treated with laser toning for melasma. The exact etiology of this complication is not known.

In one study, the authors indicate hypopigmentation might be due to the destruction of melanocytes. The number of melanocytes was reduced in the hypopigmented lesion. However, they did not compare the number of melanocytes in normally pigmented skin.[52]

A study by Ryu and Kim[53] described a case of toning-induced hypopigmentation that had decreased number of functional melanocytes on histology but normal melanocyte number.[53] Similar finding was also

reported by Wong *et al.*[54] in one Chinese patient who has received 40–50 sessions over a 6-month period.

Sugawara *et al.* studied the influence of the frequency of laser toning on the occurrence of hypopigmentation. They divided 147 patients into 3 groups and treated either weekly, biweekly, or monthly frequency. They reported that an overall incidence of hypopigmentation was 2% without any significant statistical difference in the different group. They also advised using UV imaging for early diagnosis of leukoderma.[55]

Tian[56] reviewed 23 patients of melasma who underwent biweekly toning for the period of 2 months and noticed confetti-like hypopigmentation in all of them. He recommended the frequency of treatment every 2 weeks.[56]

Laser-toning-induced hypopigmentation in patients with melasma generally does not respond well to treatment. Such hypopigmentation often persists for many years despite a variety of topical and phototherapy treatments. Various treatment options such as topical steroids, topical tacrolimus, narrowband UVB therapy, and TCA CROSS have been tried with limited success.[57]

Conclusion

Laser toning has become an extremely popular procedure in recent years. Various studies point out that it is moderately effective in the management of melasma and is not free from side effects. There is no marker predictive of successful outcome while choosing the patient for the treatment, and hence patients should be properly counseled before starting the treatment.

Authors have used laser toning in those patients who failed to respond all standard lines of treatment, and got mixed results [Figures 1–5]. In the authors experience, laser toning with 1064-nm QSL with a spot size of 10 mm,

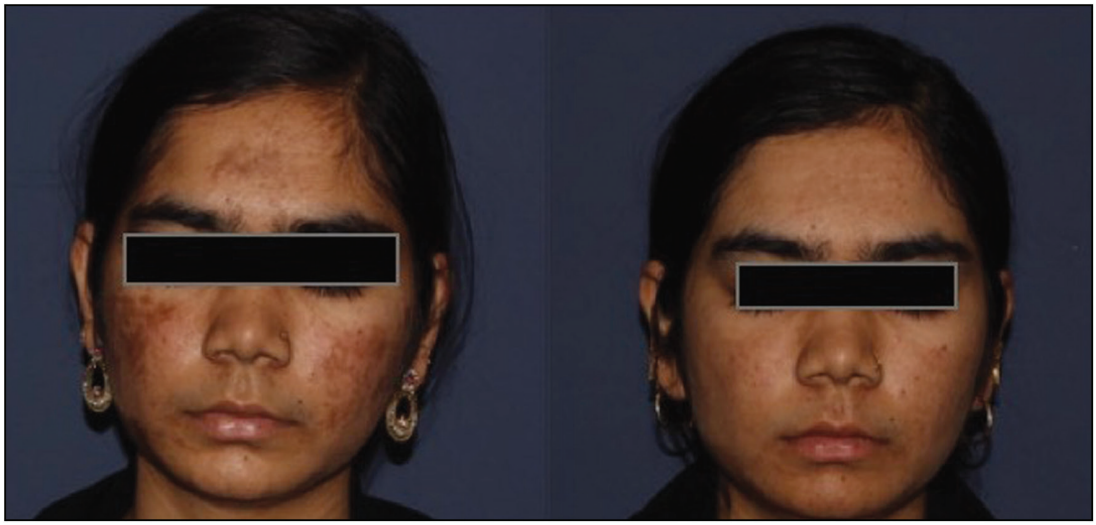

Figure 1: Excellent response to laser toning after nine sessions

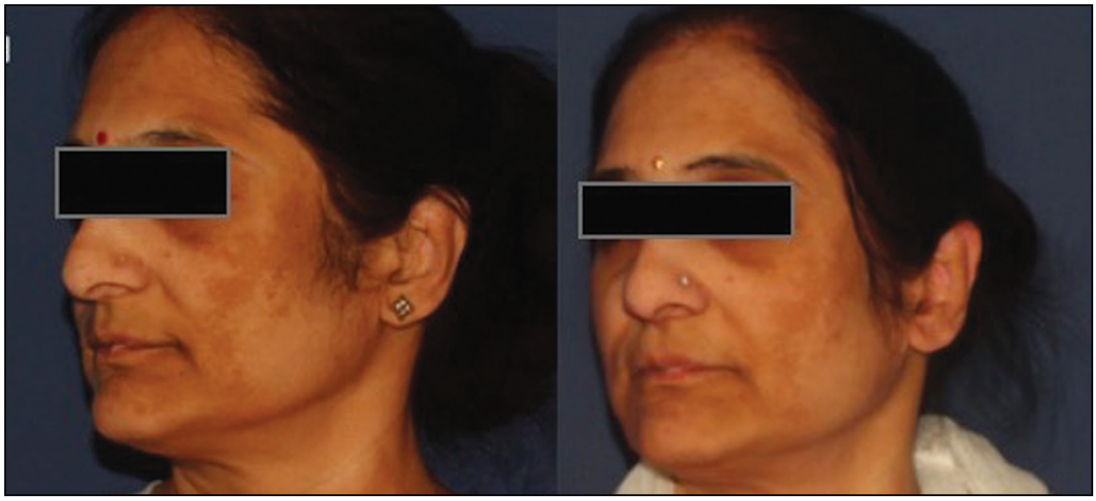

Figure 2: Moderate response to refractory melasma after 10 sessions of toning

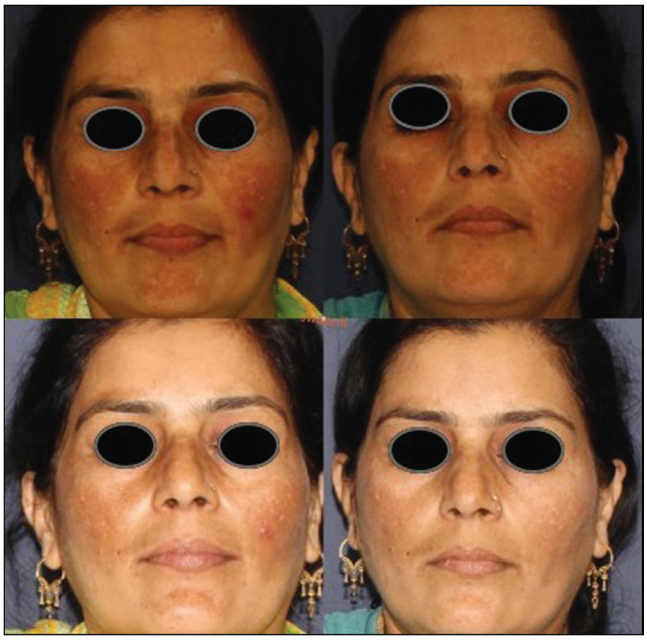

Figure 3: Moderate response to refractory melasma after six sessions of toning + microneedling + topical vitamin C

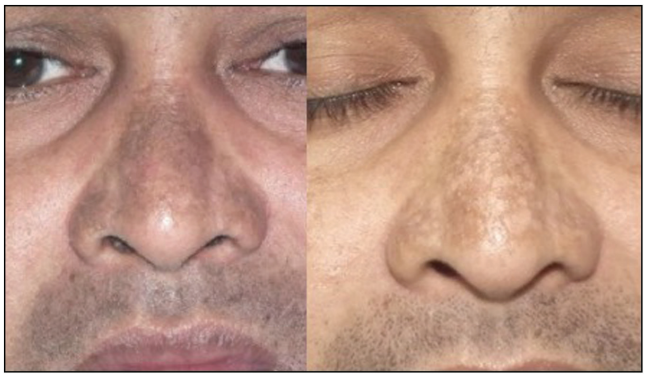

Figure 4: Mottled hypopigmentation due to toning after six sessions

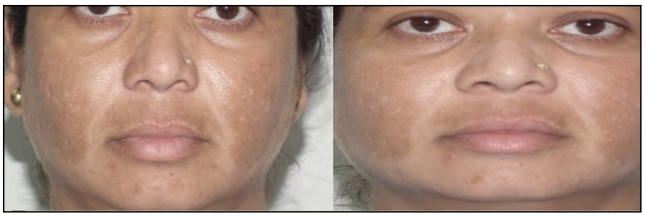

Figure 5: No response to melasma after 12 sessions

fluence of 0.85–1.2 J/cm^2, 10-Hz repetition rate, multiple passes (average 3–4) performed once in 15 days for a total of 8–10 sessions yields good results. The chances of hypopigmentation are minimal with the use of 10-mm spot size and minimal overlap of pulses. The authors also combine either dual toning (quasi-long pulse and laser toning) or gold toning (585-nm QSL with laser toning in selected cases with reasonably good outcomes.

The Indian study group has recommended combination therapy as a third-line of treatment in melasma and it should be strictly followed in day-to-day practice.[7]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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