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The effectiveness of intense pulsed light (IPL) has been reported in adults with melasma, but there is little information about IPL with triple combination topical therapy (TC) and refractory melasma. Sixty-two patients with totally or partially refractory melasma were enrolled in this randomized open-label study. Thirty-one patients were treated with IPL in a single session, bleaching agents and broad-spectrum sunscreens. Thirty-one patients were in the control group, receiving only bleaching agents and broad-spectrum sunscreens. The Melasma Area and Severity Index (MASI) and the investigator's global assessment using a seven-point scale were used to determine the impact and effectiveness of the treatment. The IPL group results based on MASI showed a 49.4% reduction (from 17.6 to 8.9; $p < 0.001$) after six months and a 44.9% reduction after 12 months (from 17.6 to 9.7; $p < 0.001$). The investigator's global assessment showed that the difference in the improvement rate between the IPL group and control group was significant ($p = 0.002$), with a better response in the IPL group. Single session IPL combined with stable fixed-dose triple combination treatment is a safe and effective treatment for refractory mixed and dermal melasma.

dermal melasma, mixed melasma, treatment

Intense pulsed light (IPL) is a noncoherent broad-spectrum light, ranging from 500 to 1200 nm, permitting the treatment of multiple conditions (1,2). For pigment disorders, IPL is associated with fewer photothermal injuries and fewer side effects than laser (3–5). Melasma is classified according to clinical

and histological features. The location of the pigment can be epidermal, dermal, or mixed. This classification is particularly important to define the therapeutic choice and the prognosis (3,4). Routine treatment, including broad-spectrum sunscreens, and bleaching agents, such as hydroquinone, tretinoin, and chemical peels, have shown satisfactory results in patients with epidermal melasma (4). Nevertheless, patients with dermal or mixed-type melasma are therapeutically challenging (6). A previous study has indicated the use of IPL in refractory melasma, showing a therapeutic success rate of 70–77% (4,6). The present study aims to clarify the effect of IPL on melasma refractory to

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stable fixed-dose triple combination treatment (hydroquinone 4%, tretinoin 0.05%, fluocinolone acetonide 0.01%) in skin phototypes II–V.

Sixty-two patients with melasma totally or partially resistant to 6 months of treatment with combined bleaching agents were enrolled in this randomized, evaluator-blinded, open-label study. Patients with mixed or dermal melasma, phototypes II–V, resistant to the triple combination treatment (TC) were included. All patients were assessed by dermoscopy (video dermatoscope, Castells, Sao Paulo, Brazil). Melasma was considered to be of the epidermal type (brownish homogeneous pigmentation and a regular pigmented network), the dermal type (bluish gray pigmentation and an irregular network), or mixed (areas presenting both features) (7). The exclusion criteria for the present study included pregnancy, patients with epidermal melasma, lactation, use of oral contraceptives, hormone replacement therapy, potentially photosensitizing drugs, and major outdoor activities. Patients underwent a clinical evaluation using the Melasma Area and Severity Index (MASI) (8,9). An investigator's global assessment of improvement was used, which was based on a 7-point scale, from 1 (worst) to 7 (clear). The investigator's global assessment and MASI readings were taken by the same investigators at each time point. All patients were assigned with individual identification numbers and were randomly and equally divided into two groups (IPL and control) using a random numbers table. Thirty-one patients in the IPL group were treated with IPL with a cooling device, real-time calibration, and automatic pulse (Limelight, Cutera, Brisbane, CA, USA) in a single session with a filter of 560 nm and fluencies ranging from 12 to 22 J to skin phototypes II–V. Most patients complained of mild to moderate pain and a burning sensation. Immediately after treatment, some mild, transient erythema was present. This was followed by slight darkening of the pigmented lesions, the gold standard indication of the treatment. IPL group patients developed microcrusts and were treated with fusidic acid associated with Betamethasone Valerate Cream, aciclovir 400 mg/day for 10 days, deflazacort 30 mg/day for 5 days, and broad-spectrum sunscreens until disappearance, which occurred between 1 and 2 weeks. Then, the use of bleaching agents (stable fixed-dose triple combination treatment) that had previously been totally or partially refractory was restarted in IPL group as a means of

avoiding possible repigmentation. Evaluations by MASI were performed in the first and sixth months and, later, a final evaluation was performed at the end of the twelfth month. Thirty-one patients were in the control group, receiving only triple combination treatment and broad-spectrum sunscreens. Statistical analysis was performed using *t*-tests, paired *t*-tests. All values were expressed as means $\pm$ standard deviation (SD). A *p* value less than 0.05 was considered as statistically significant. Informed consent was obtained. The present study was conducted according to the Declaration of Helsinki.

A total of 62 patients (58 women and 4 men; mean $\pm$ SD age 44.3 ± 6.1 years) were evaluated in the study. The variables of age, phototypes II, III, IV, or V, type of refractory melasma (mixed or dermal), and duration of the melasma were not significant (Table 1). Racial background was reported as white in 28 (45.2%) of the patients, mixed in 26 (41.9%), and black in 8 (12.9%). Twelve patients in the control group dropped out because of poor response. The IPL group results based on MASI scoring after 6 months showed a 49.4% reduction (from 17.6 to 8.9; $p < 0.001$); after 12 months, a 44.9% reduction was observed (from 17.6 to 9.7; $p < 0.001$). Ten IPL group patients with frontal and malar melasma showed clinical improvement of the lesions, but the assessments by MASI were not statistically significant ($p = 0.054$); 21 IPL group patients with melasma without the presence of lesions on the forehead showed statistically significant improvement ($p < 0.001$). The investigator's global assessment (Table 2) showed that the difference in the improvement rate between IPL group and control group was significant ($p = 0.002$), with a better response in the IPL group (FIG. 1). Few side effects were associated with IPL treatment. No wounds, infection, or scar formation were noted. Erythema and pain during and after treatment were mild and disappeared within 1 day. There were three cases of skin phototype IV patients with malar melasma treated with a fluency of 18 J who presented post-inflammatory hyperpigmentation that completely improved with continuous use of bleaching agents within 4–6 months.

IPL is a noncoherent broad-spectrum light permitting the treatment of multiple conditions. Treatment of melasma only with TC has resulted in 77%

1. Characteristic of refractory melasma patients and treatment response

Data	Group	
	Intense pulsed light	Control
Age (years)	43.8 ± 7.2	45.1 ± 4.3
Duration (years)	8.9 ± 4.2	9.4 ± 4.8
Skin phototypes	II = 3, III = 11	II = 4, III = 10
	IV = 13, V = 4	IV = 13, V = 4
Type	Mixed = 19	Mixed = 17
	Dermal = 12	Dermal = 14
Melasma area and severity index		
Baseline	17.6 ± 6.5 (<i>n</i> = 31)	16.5 ± 4.9 (<i>n</i> = 31)
6 months	8.9 ± 6.8 (<i>n</i> = 31) ^{a,b}	16.1 ± 5.6 (<i>n</i> = 19) ^b
12 months	9.7 ± 5.9 (<i>n</i> = 31) ^c	— ^d

^aImprovement within the group (paired *t*-test), *p* < 0.001.

^bDifference between the intense pulsed light and control group (*t*-test), *p* = 0.002.

^cImprovement within the group (paired *t*-test), *p* < 0.001.

^dNot done.

2. Investigator's global assessment with a 7-point scale

Rating	After treatment			
	6th month		12th month	
	<i>n</i> (%)		<i>n</i> (%)	
	IPL group	Control group ^a	IPL group	Control group ^b
	31 (100)	19 (100)	31 (100)	—
Worst	1 (3.2)	9 (47.4)	0 (0)	—
No change	3 (9.7)	2 (10.5)	4 (12.9)	—
Slight	6 (19.4)	5 (26.3)	7 (22.6)	—
Moderate	8 (25.8)	3 (15.8)	12 (38.7)	—
Marked	10 (32.3)	0 (0)	8 (25.8)	—
Almost clear	3 (9.7)	0 (0)	0 (0)	—
Clear	0 (0)	0 (0)	0 (0)	—

^aTwelve patients in group B dropped out because of poor response.

^bDropped out or changed treatment.

IPL, intense pulsed light.

of patients being clear or almost clear after 8 weeks of treatment (6). The present study showed that single-session IPL followed by TC was more effective than TC cream therapy alone for mixed and dermal melasma treatment. Additionally, the correct use of bleaching agents only in pigmented areas, avoiding contact with normal skin as much as possible, facilitates the use of IPL in refractory melasmas. The improvement after one session of IPL was 49.4%, significantly higher when compared with another study that showed an improvement of 24.9% compared with baseline (4). The use of TC after the disappearance of microcrusts reduced treatment failure compared with another study (4). Nevertheless, patients with frontal and malar melasma showed a poor response, and patients with melasma without the presence of lesions on the forehead showed a statistically significant

improvement. The present study showed a lower frequency of excellent improvement (almost clear and clear) than can be found in the literature, probably due to the use of a single IPL session (10). The MASI scores revealed the effectiveness of IPL in treating pigmented lesions of low and high contrasts with promising results. Effective treatments in Hispanics and Asians have been performed using IPL with few adverse effects (5,11). Furthermore, other treatments, such as Er:YAG lasers, dermabrasion, ultrapulse CO₂ lasers, and fractional lasers, have demonstrated effects on melasma. Nevertheless, they are more aggressive or high-cost methods, a larger number of sessions are required to obtain satisfactory results, and there tends to be in some cases the occurrence of persistent erythema, post-inflammatory hyperpigmentation, or scarring (12–15).



Fig. 1. (a) Pre-treatment (b) Post-treatment (c) Pre-treatment (d) Post-treatment

In conclusion, single-session IPL combined with stable fixed-dose triple combination treatment is a safe and effective treatment for refractory mixed and dermal melasma. Patients with frontal and malar melasma showed a poor response, and patients with melasma without the presence of lesions on the forehead showed a statistically significant improvement. IPL stands out as an effective tool in the refractory melasma treatment, with minimal side effects when done under the correct conditions.

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