Melasma Treatment With Pulsed-Dye Laser and Triple Combination Cream: A Prospective, Randomized, Single-Blind, Split-Face Study

Recent data show that melasma lesions have, in addition to increased pigmentation, more elastosis and vascularization than perilesional skin.1-3 The stabilized formulation of Kligman preparation has shown significant improvements in the treatment of melasma.4 However, most of the treatments only target the pigmentation, and none of them has been demonstrated so far to prevent the frequent relapses.

Pulsed-dye laser treatment (PDL) is considered the gold standard therapy for vascular lesions. By targeting not only melanin but also vascularization and at least in part elastosis, PDL might provide, in combination with blanching cream, an effective and complete therapeutic approach for melasma. The objective of this pilot study was to evaluate the dual treatment of fixed triple combination cream (TCC) and PDL in the treatment of melasma.

Methods. We conducted a controlled, randomized, single-blind, split-face clinical trial. Patients seeking treatment for melasma were included. Exclusion criteria were skin phototype V, medical history of allergy to the compounds of the TCC, or current pregnancy or breastfeeding.

All patients applied to the entire face the TCC containing hydroquinone, 4%; tretinoin, 0.05%; and fluocinolone acetonide, 0.01% (Tri-Luma Cream; Galderma Laboratories LP, Fort Worth, Texas), once a day for 4 months. The PDL treatment (Vbeam; Candela Corporation, Wayland, Massachusetts) was started after 1 month of TCC applications. Three sessions of PDL were performed at 3-week intervals on the half face that was randomly assigned. For each session, a first passage was performed on melasma lesions aiming at removing the hyperpigmentation (compression handpiece of 10 mm; pulse duration, 1.5 milliseconds; fluency, 7 J/cm²). A second passage was performed immediately afterwards, using a regular handpiece of 7 mm in diameter on the entire hemiface with a 10% overlap of treatment spots to target the vessels (pulse duration, 20 milliseconds; fluency, 10 J/cm²; dynamic cooling device, 30/40). All the patients were told to apply the entire face a sunscreen of sun protection factor 50 or higher (combining Mexoryl SX and XL; L’Oreal, Paris, France) during the entire study duration.

The main criterion of evaluation was the Melasma Area and Severity Index (MASI)5 calculated by an independent physician blinded to treatment on standardized digital photographs (VISIA; Canfield Imaging Systems, Fairfield, New Jersey). Tolerance and satisfaction were graded by the patients on a visual analog scale (VAS). To avoid confusion of results possibly caused by spontaneous improvement of melasma that is usually observed during autumn and winter months, all the patients were included at the end of winter season and a final visit was scheduled after the summer, at least 2 months after the last treatment.

Table. Comparisons of MASI Scoresa Between Treatment Types and Evaluation Timesb

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>Before Treatment</th>
<th>End of Treatment</th>
<th>P Valuec</th>
<th>Follow-up Visit After 1 Summer</th>
<th>P Valued</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (n = 17)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>TCC</td>
<td>6.76 (3.25)</td>
<td>4.35 (2.76)</td>
<td>.003</td>
<td>6.06 (3.86)</td>
<td>.13</td>
</tr>
<tr>
<td>TCC plus PDL</td>
<td>6.20 (3.02)</td>
<td>2.79 (2.70)</td>
<td>.001</td>
<td>4.15 (3.89)</td>
<td>.01</td>
</tr>
<tr>
<td>Phototypes II or III (n = 11)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCC</td>
<td>6.31 (2.98)</td>
<td>4.02 (2.62)</td>
<td>.03</td>
<td>5.46 (3.88)</td>
<td>.23</td>
</tr>
<tr>
<td>TCC plus PDL</td>
<td>5.36 (2.62)</td>
<td>1.72 (1.12)</td>
<td>.003</td>
<td>2.25 (2.44)</td>
<td>.01</td>
</tr>
<tr>
<td>Phototype IV (n = 6)</td>
<td></td>
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<td></td>
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<tr>
<td>TCC</td>
<td>7.65 (3.88)</td>
<td>4.96 (3.15)</td>
<td>.03</td>
<td>7.14 (3.93)</td>
<td>.35</td>
</tr>
<tr>
<td>TCC plus PDL</td>
<td>7.90 (3.28)</td>
<td>4.74 (3.69)</td>
<td>.046</td>
<td>7.64 (3.73)</td>
<td>.67</td>
</tr>
</tbody>
</table>

Abbreviations: A, area involved; D, darkness; H, homogeneity; MASI, Melasma Area and Severity Index; PDL, pulsed-dye laser; TCC, triple combination cream containing hydroquinone, 4%; tretinoin, 0.05%, and fluocinolone acetonide, 0.01% (Tri-Luma Cream; Galderma Laboratories LP, Fort Worth, Texas).

a Hemi-MASI score was calculated for each side of the face as follows: forehead, 0.15 × (D+H) × A + malar, 0.30 × (D+H) × A + chin, 0.05 × (D+H) × A.
b Unless otherwise indicated, data are reported as mean (SD) MASI scores.
c P value for within-group comparisons between before-treatment and end-of-treatment groups.
d P value for within-group comparisons between before-treatment and follow-up visit after summer group.
e P value for between-group comparisons; to account for multiple comparisons, P values were considered significant at P < .025.
tation (PIH) was observed in 3 patients, all phototype IV, treated with PDL.

Comment. The use of PDL in association with a bleaching cream appears beneficial in treating melasma in patients with skin phototypes II and III. Hyperpigmentation is not homogeneous in melasma, and the split-face trial design may have deficiencies in detecting improvement. However, not only did the between-group comparisons show statistical differences, but the within-group comparisons showed significant differences after the summer compared with the initial score for the PDL-treated side, while the difference was no longer significant in the group treated with only the cream. Those data strongly support the beneficial effect of the PDL treatment despite the heterogeneity of the hyperpigmentation. Half of the patients with dark skin developed a PIH. The use of a PDL passage to target the melanin and to try enhancing the depigmentation might be responsible for the high percentage of PIH in dark-skinned patients. This pass targeting melanin should not be used for further studies.

To our knowledge, this is the first time that a treatment has been shown to prevent, at least partially, relapse of melasma. Melanocytes express vascular endothelial growth factor (VEGF) receptors 1 and 2 and neuropilin. Thus, the VEGF and skin vascularization might play a role in the pigmentation processes and therefore in melasma. By targeting the vascular component in melasma lesions, the PDL may decrease the melanocyte stimulation and subsequently the relapses. These results emphasize the necessity for a broader approach for melasma treatment targeting all components of this complex disorder. Additional studies with several years of follow-up are now required to draw definitive conclusions about the prevention of relapses and to determine the optimal parameters and schedule of treatment.

Figure. Clinical photographs of the forehead taken under UV light before treatment (A), at the end of the treatment (B), and after 1 summer (C). Left side of the patient’s face has been treated with the triple combination cream, right side with both the cream and pulsed-dye laser.

Between- and within-group comparisons of hemifacial MASI scores as well as analyses of tolerance and patient satisfaction were performed using the Wilcoxon signed-rank test (SPSS software, version 11.0; SPSS Inc, Chicago, Illinois).

Results. Eighteen patients, all white women, were included (4 skin phototype II; 8 phototype III; and 6 phototype IV). One patient dropped out after 1 month of treatment for professional reasons. The mean age was 41 years (range, 33-56 years). The results are summarized in the Table. The Figure shows the clinical appearance of 1 patient before treatment, after treatment, and after 1 summer. Tolerance of the cream alone was excellent (9.3 of 10) and good when the laser was added (7.3 of 10) ($P<.001$), while patient satisfaction was graded at 6 of 10 for the cream alone and 7.1 of 10 for the combined approach ($P<.05$). Patient satisfaction was significantly greater for the combination treatment in patients with skin phototypes II and III ($P<.01$), while no significant differences between the 2 treatment groups were reported for phototype IV. A transient and mild irritation due to the cream was reported by half of the patients. Postinflammatory hyperpigmentation (PIH) was observed in 3 patients, all phototype IV, treated with PDL.

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script for important intellectual content: Passeron, Fontas, Kang, Bahadoran, Lacour, and Ortonne. Statistical analysis: Fontas. Obtained funding: Passeron and Ortonne. Administrative, technical, and material support: Lacour and Ortonne. Study supervision: Passeron.

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A Randomized Split-Scar Study of Intraoperative Treatment of Surgical Wound Edges to Minimize Scarring

For ablative resurfacing of surgical scars, the recommended time frame for treatment has remained relatively constant at 8 weeks postoperatively.1 However, Strauss and Kligman2 were aware as early as 1956 that dermabrasion to the wound edges at time of closure would improve the final appearance of sutured wounds. In 1980, Caver3 reported that dermabrasion to wound edges at the time of surgery had been used successfully in his practice for over 20 years. In recent years, 2 studies using ablative laser resurfacing of wounds at the time of closure have shown promising trends.4,5 Ablative fractional resurfacing has been shown to quantitatively improve atrophic surgical and traumatic scars.6

The improved safety profile of fractional carbon dioxide lasers vs their fully ablative counterparts and the ability to treat nonfacial sites makes them well suited for scar treatments. Our study aims to quantify the improvements resulting from intraoperative fractional carbon dioxide laser treatment. To our knowledge, this is the first prospective fractional laser study for this indication and the first to evaluate nonfacial sites.

Methods. This study was approved by Western Institutional Review Board, Olympia, Washington. Ten subjects were enrolled. Patients were recruited when a linear complex closure longer than 2.0 cm was planned for repair after excisional surgery.

The surgical defects were divided into 2 halves along the planned closure axis. After the subcuticular 4.0 buried sutures were placed (Vicryl; Ethicon Inc, Somer-