Outcomes of Childhood Hemangiomas Treated with the Pulsed-Dye Laser with Dynamic Cooling: A Retrospective Chart Analysis

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BACKGROUND Laser treatment of childhood hemangiomas remains controversial. Previous studies have used outdated technology, resulting in a potential overrepresentation of adverse outcomes.

OBJECTIVE To evaluate outcomes of hemangiomas treated with the most current laser technology.

METHODS A retrospective chart analysis of 90 patients with a median age of 3.0 months and a total of 105 hemangiomas were enrolled over a 2.5-year period. All were treated with the 595-nm long-pulse pulsed-dye laser (LP-PDL) with dynamic epidermal cooling at 2- to 8-week intervals depending on the stage of growth. Exclusion criteria were previous laser, surgical, or corticosteroid treatment. Three reviewers assessed outcomes.

RESULTS Near-complete or complete clearance in color were achieved for 85 (81%) and in thickness for 67 (64%) hemangiomas. There was no scarring or atrophy. Ulceration occurred in one case and resolved during treatment. Hyperpigmentation and hypopigmentation occurred in 4% and 14% of hemangiomas, respectively.

CONCLUSION Early treatment of childhood hemangiomas with the 595-nm LP-PDL with dynamic cooling may reduce the proliferative phase and result in excellent rates of clearing and few adverse events.

Dr. Geronemus serves on the Advisory Board for Candela Corporation.

Hemangiomas are vascular tumors affecting up to 5% to 10% of infants. The lesions are present at birth or develop shortly after and are characterized by a sequence of rapid proliferation, stabilization, and slow involution. Conservative management is often initially favored because of the potential for spontaneous involution, although the behavior of individual hemangiomas is heterogeneous, making it difficult to predict outcomes reliably. Approximately 20% of hemangiomas result in pain, bleeding, ulceration, infection, or functional impairment with vision, feeding, or breathing necessitating medical or surgical treatment.1 Involution is incomplete by the start of school in 50% of children, and even after spontaneous involution, 15% to 40% of children are left with skin changes, including pigmentary alteration, telangiectasia, and atrophy, as well as fibro-fatty residuum often necessitating surgical correction.2,3 Treatment of early hemangiomas with laser therapy may hasten the involutional process and improve rates of complete clinical clearance, but published studies have not shown consistent benefits, and laser treatment of hemangiomas has remained controversial. This is due in part to a lag in the use and evaluation of the most advanced laser technology, resulting in an overreporting of adverse outcomes due to thermally induced epidermal damage.

The long-pulse pulsed-dye laser (LP-PDL), with a wavelength of 595 nm and the addition of dynamic epidermal cooling, has become the standard of care for treatment of port wine stains. This modality has

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© 2009 by the American Society for Dermatologic Surgery, Inc. • Published by Wiley Periodicals, Inc. • ISSN: 1076-0512 • Dermatol Surg 2009;35:1–8 • DOI: 10.1111/j.1524-4725.2009.01356.x
proven effective in the treatment of ulcerated hemangiomas, and the addition of epidermal cooling has been demonstrated to decrease the frequency of adverse events when used in combination with long pulse widths, although to our knowledge, no published outcomes are available evaluating the application of this updated technology at standard pulse widths for the treatment of uncomplicated infantile hemangiomas. This retrospective chart analysis was undertaken to assess the rate of clearing and adverse events including atrophy, scarring, ulceration, and pigmented changes of early hemangiomas treated with the 595-nm-wavelength LP-PDL with dynamic cooling.

Patients and Methods

The records of all consecutive hemangioma patients treated with LP-PDL for superficial or mixed superficial and deep hemangiomas in a laser surgery clinic specializing in the treatment of vascular lesions from January 2005 to September 2007 were screened against eligibility criteria. Inclusion required the treatment of a superficial or mixed hemangioma with the 595-nm LP-PDL with dynamic cooling. Exclusion criteria were previous laser or surgical intervention or previous or concomitant treatment with intralesional or systemic corticosteroids. One patient was excluded because of the poor quality of photographic documentation. The parents of all patients gave written informed consent for photography and participation in clinical research before inclusion, and the Essex institutional review board, Essex, New Jersey, approved the study protocol.

A total of 90 patients with 105 hemangiomas were included. Ten patients had two hemangiomas, one had three, and one had four separate lesions; the remainder had only one lesion. Characteristics of the patients (age at onset of treatment, sex, Fitzpatrick skin type) and clinical characteristics of the hemangioma (type, size, location, presence of ulceration at onset of treatment) are shown in Table 1. Hemangiomas were divided into two groups based on the presence or absence of a subcutaneous component; 65 superficial hemangiomas and 40 mixed lesions were identified. Fifty-two percent of superficial hemangiomas were actively growing at the onset of treatment, 40% had plateaued but not begun to involute, and 7% were involuntional. Of the mixed hemangiomas, 65% were actively growing, 20%...
plateaued, and 11% were involutional. No hemangiomas had completely involuted before the start of treatment. Ulceration was present at the time of initial evaluation before the initiation of laser therapy for three superficial and four mixed hemangiomas.

A 595-nm LP-PDL (V-Beam Perfecta, Candela Corp, Wayland, MA) associated with a dynamic skin cooling system was used for all treatments. A spot size of 7 or 10 mm was used with an average energy fluence of 11.5 J/cm² (range 7.5–14.0 J/cm²) or 8.6 J/cm² (range 6.2–11.5 J/cm²), respectively. Energy fluence varied according to patient and hemangioma characteristics, including age, skin type, location, lesion thickness, and response to previous treatments. Pulse duration was 0.45 or 1.5 ms depending on the response to prior treatments and anticipated size of target vessels. Dynamic cooling device spray with a duration of 30 ms was applied before each laser pulse, followed by a 30-ms post-laser pulse delay. Treatments were performed with a spot overlap of 0% to 20% as needed to achieve purpura of the entire lesion. Darker skin types were treated with less spot overlap to minimize the risk of epidermal damage. Almost all hemangiomas were treated without anesthesia, with topical anesthetic applied before treatment of larger lesions only for patients aged 1 year and older. For the treatment of lesions near the orbit, metal eye shields were applied after corneal anesthesia with tetracaine 0.7% solution eye drops. Parents were instructed to avoid trauma and sun exposure to treated areas and to apply hydrophilic ointment if crusting developed.

Treatments were repeated at 2- to 8-week intervals, depending on patient compliance with the treatment schedule and stage of growth; actively growing hemangiomas were treated at 2-week intervals to help minimize regrowth between treatment sessions, whereas lesions that had plateaued were treated at longer intervals of 4 to 6 weeks. Treatments were continued until the lesion cleared or stopped responding or the parent discontinued treatment.

Standardized clinical photographs were taken on the date of initial evaluation and before each treatment. Three reviewers (AMC, EKH and JLC) with specialties in dermatologic laser surgery or pediatric dermatology independently assessed initial, intermediate, and final treatment photographs. No standardized or validated method exists for outcomes measurement of hemangiomas. To facilitate comparison, we chose a rating method similar to that employed in other hemangioma studies. Improvement in color and lesion thickness were graded as none (0%), minimal (1–24%), fair (25–49%), moderate (50–75%), near complete (76–99%) or complete (100%) resolution. Average values were calculated when reviewer assessment differed. The presence or absence of scarring, atrophy, pigmentary changes, and ulceration were documented when at least two of three independent reviewers identified them. The unpaired Student t-test was used to analyze the relationship between age at start of treatment, number of laser treatments, and duration of follow-up and primary and secondary outcomes.

Results

Ninety patients with 105 hemangiomas treated with the LP-PDL were evaluated. Mean duration of follow-up was 9.3 months (range 1–72 months): 8.1 months for superficial and 11.4 months for mixed hemangiomas. The mean number of treatments ± standard deviation was 6.7 ± 4.5: 5.8 ± 4.2 for superficial and 8.0 ± 4.7 for mixed hemangiomas. The number of laser treatments per child is shown in Figure 1; overall, 28% of participants required three or fewer treatments, 72% required seven or fewer treatments, and 11% underwent more than 12 treatments.

Table 2 shows the improvement in color and thickness at the conclusion of treatment. Fifteen of 65 (23%) superficial hemangiomas demonstrated complete clearance in color, and 38 (58%) demonstrated near-complete clearance; only two (3%) demonstrated minimal clearance. Of 40 mixed superficial and deep hemangiomas, six (15%) demonstrated
complete clearance of color, 26 (65%) demonstrated near-complete clearance, and three (8%) had minimal change. Altogether, 81% of hemangiomas demonstrated better than 75% clearance of color.

Improvement in the thickness of hemangiomas was separately assessed. Of 65 superficial hemangiomas, 13 (20%) demonstrated no residual thickness, and 38 (58%) demonstrated near-complete resolution of thickness at the conclusion of treatment. Only two (3%) superficial hemangiomas demonstrated minimal change in thickness. Of 40 mixed superficial and deep hemangiomas, only three (8%) demonstrated complete resolution of thickness, and 13 (33%) demonstrated near-complete clearance. No improvement was noted in one lesion, and 11 (28%) had minimal change in thickness. Overall, 64% of hemangiomas demonstrated near-complete or complete resolution in thickness. Representative cases of complete and near-complete clearance of color and thickness of superficial and mixed hemangiomas are shown in Figures 2 and 3, respectively. Age at start of treatment, lesion size, duration of follow-up, and number of laser treatments were not significantly correlated with clearance rates (data not shown).

Adverse events are shown in Table 3. There were no cases of atrophy or hypertrophic scarring. There was only one case of minor ulceration that developed after the onset of treatment and thus potentially could be a result of laser therapy. Ulceration was present at initial evaluation, before the onset of treatment, for three superficial and four mixed hemangiomas. All ulcers resolved without scarring during the course of treatment and did not require treatment to be stopped or delayed. On the date of final treatment, hyperpigmentation was noted in four (6%) patients with superficial hemangiomas.

TABLE 2. Primary Outcome Measures at the Completion of Treatment with the Long-Pulse Pulsed-Dye Laser with Dynamic Cooling

<table>
<thead>
<tr>
<th></th>
<th>Superficial (n = 65)</th>
<th>Mixed (n = 40)</th>
<th>Total (n = 105)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Color</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete (100%)</td>
<td>15 (23)</td>
<td>6 (15)</td>
<td>21 (20)</td>
</tr>
<tr>
<td>Near complete (75–99%)</td>
<td>38 (58)</td>
<td>26 (65)</td>
<td>64 (61)</td>
</tr>
<tr>
<td>Moderate (50–74%)</td>
<td>9 (14)</td>
<td>3 (8)</td>
<td>12 (11)</td>
</tr>
<tr>
<td>Fair (25–49%)</td>
<td>1 (2)</td>
<td>2 (5)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Minimal (1–25)</td>
<td>2 (3)</td>
<td>3 (8)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>None (0%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>Thickness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete (100%)</td>
<td>13 (20)</td>
<td>3 (8)</td>
<td>16 (15)</td>
</tr>
<tr>
<td>Near complete (75–99%)</td>
<td>38 (58)</td>
<td>13 (33)</td>
<td>51 (49)</td>
</tr>
<tr>
<td>Moderate (50–74%)</td>
<td>10 (15)</td>
<td>4 (10)</td>
<td>14 (13)</td>
</tr>
<tr>
<td>Fair (25–49%)</td>
<td>2 (3)</td>
<td>8 (20)</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Minimal (1–25)</td>
<td>2 (3)</td>
<td>11 (28)</td>
<td>13 (12)</td>
</tr>
<tr>
<td>None (0%)</td>
<td>0 (0)</td>
<td>1 (3)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

Three independent reviewers evaluated cases, and averages were used in cases in which reviewer assessment differed. Percentages may total more or less than 100 because of rounding.
There were no cases of hyperpigmentation in patients with mixed lesions. Hypopigmentation was present on the date of final treatment in 10 (15%) and five (13%) patients with superficial and mixed hemangiomas, respectively. Dyspigmentation was not correlated with Fitzpatrick skin type. The development of hypopigmentation was significantly associated with a greater number of laser treatments, with a mean of 9.1 ± 5.5 in the group with hypopigmentation, compared with 6.3 ± 4.2 in those without (p = .03). Because these treatments were administered at 2- to 6-week intervals, these patients were necessarily followed for a longer duration of time: an average of 17.3 ± 18.6 months in the group with hypopigmentation, compared with 8.0 ± 8.9 months in the group without (p < .003). Hyperpigmentation, in contrast, was associated with fewer treatments over a shorter duration of time: an average of 4.2 ± 1.0 treatments over 2.7 ± 1.0 months in the group with hyperpigmentation, compared with 6.8 ± 4.6 treatments over 9.6 ± 11.3 months in the group without hyperpigmentation, which did not reach statistical significance (p = .27 for number of treatments, p = .23 for duration of follow-up).

Because clinical photographs were not taken after the date of final treatment, we were not able to determine the persistence of these pigmentary changes.

Discussion

It has been suggested that early treatment of infantile hemangiomas with the LP-PDL hastens involution and resolution. This treatment modality has shown exceptional success and safety in the treatment of port wine stains and has rapidly become first-line treatment of these lesions, but optimization of hemangioma treatment has proven more challenging, and laser intervention remains controversial. This is largely because of the distinct characteristics of hemangiomas, which are rapidly proliferating tumors of densely packed small vessels with little interspersed dermis and significant depth, presenting a challenge for optimal laser targeting. It is also due in part to the unpredictable behavior of individual hemangiomas making it difficult to reliably assign outcomes to treatment rather than the natural history of the tumor.

The goal of laser treatment of hemangiomas is to maximize vascular damage while minimizing non-specific injury to interspersed dermis and overlying epidermis. The combination of pulse duration, spot size, and wavelength determines the effect of laser treatment on cutaneous blood vessels. Earlier pulsed-dye lasers (PDLs) had a wavelength of 585 nm, corresponding to an absorption peak of hemoglobin. More recently, LP-PDLs with wavelengths of 595 nm have enabled greater depth of vascular injury while maintaining chromophore selectivity. Previous studies employing the 585-nm PDL with a pulse width of 0.45 ms or less have shown disappointing results in the treatment of hemangiomas with a subcutaneous component. The LP-PDL with dynamic cooling employing a 595-nm wavelength and pulse widths of up to 1.5 ms allows better targeting of the deeper component of hemangiomas.
In 2002, Batta and colleagues published the first randomized controlled trial comparing no intervention with early treatment with the 585-nm PDL without epidermal cooling for superficial childhood hemangiomas. The study showed that early treatment was significantly more likely to result in complete clearance of hemangiomas at 1 year of age (30% of those treated with early PDL vs only 5% of the control group, \( p < .001 \)), but the authors also reported high rates of adverse outcomes, including skin atrophy (28% of the treatment group, 8% of controls) and hypopigmentation (45% of the treat-

### Table 3. Documented Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Superficial (n = 65)</th>
<th>Mixed (n = 40)</th>
<th>Total (n = 105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperpigmentation</td>
<td>4 (6)</td>
<td>0 (0)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Hypopigmentation</td>
<td>10 (15)</td>
<td>5 (13)</td>
<td>15 (14)</td>
</tr>
<tr>
<td>Ulceration</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Atrophy</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hypertrophic scarring</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

There were no cases of atrophy or hypertrophic scarring. Ulceration reflects onset after the initiation of laser therapy.
ment group, 15% of controls), despite a predominantly Caucasian study population. These rates of hypopigmentation and atrophy are far higher than those reported in other studies, which ranged from 0% to 10% for hypopigmentation and 0% to 4% for atrophy.\(^9,10,13\) The authors also report high rates of ulceration during treatment (7%), perhaps indicating that settings were not optimized to prevent nonspecific thermal damage.

It is additionally likely that the failure to use protective epidermal cooling contributed to the high rates of adverse outcomes. Epidermal cooling systems have been designed to allow delivery of higher energy fluences to dermal vasculature while decreasing the risk of epidermal damage. The use of dynamic cooling has been shown to significantly minimize adverse events in the treatment of port wine stains\(^14\) and to result in reduction of hemangioma thickness, texture, and color after fewer laser treatments because of the ability to safely deliver greater energy.\(^4\) In a small study of Asian infants, Kono and colleagues demonstrated significantly lower rates of hypopigmentation, hyperpigmentation, and textural change with the addition of dynamic cooling to the 595-nm PDL employed at extended pulse durations of 10 to 20 ms,\(^5\) although pulse widths of this duration have not been widely used because they may not optimally affect vascular targets.

In this retrospective chart analysis, we reviewed the outcomes of childhood hemangiomas treated with the 595-nm LP-PDL with dynamic cooling at a tertiary care vascular lesion surgery center over 2.5 years to determine rates of clearance and complications. We found high rates of clearance for superficial and mixed hemangiomas. Near-complete or complete clearance of color was achieved for 82% of superficial and 80% of deep hemangiomas, and 78% and 40% demonstrated complete or near-complete resolution of the thickness, respectively. These rates of improvement in color are within previously published ranges.\(^7,9,10\) These outcomes were achieved after seven or fewer treatments for more than 70% of cases.

The most common adverse event was hypopigmentation, occurring in 14% of hemangiomas. These results are significantly lower than those reported by Batta and colleagues,\(^7\) which we attribute to relative epidermal protection from dynamic cooling. The development of hypopigmentation was associated with greater number of treatments (average of 6.3 vs 9.1 in the group without hypopigmentation, \(p = .03\)). In most cases, the date of final photographic documentation occurred at the time of the final laser treatment. Prior studies have demonstrated the transient nature of dyspigmentation occurring after laser treatment of hemangiomas;\(^9\) as such, it is likely that some resolution of dyspigmentation would have been seen had additional follow-up been possible.

There were no cases of hypertrophic scarring or atrophy. Ulceration occurred after the onset of laser treatment in one case but resolved spontaneously without scarring and did not necessitate delaying treatment. It is impossible to determine whether the dyspigmentation and rare ulceration may be attributed to the hemangioma itself or to the treatment. Regardless, with careful selection of spot size and fluence, we show that nonspecific dermal injury and subsequent atrophy can be largely avoided.

Treatment of hemangiomas with the LP-PDL with dynamic cooling may reduce the proliferative phase and hasten involution. The use of a longer wavelength in combination with dynamic cooling enables the safe application of higher fluences. This results in better targeting of deeper vessels and better clearance of the thickness of hemangiomas while minimizing the risk of dyspigmentation and atrophy. In conclusion, this study demonstrates that the use of the 595-nm-wavelength LP-PDL with dynamic cooling in the early treatment of hemangiomas results in excellent rates of clearing and relatively few adverse events.

References


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