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Beneficial Effects of Early Pulsed Dye Laser Therapy in Individuals with Infantile Hemangiomas

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Infantile hemangiomas (IH) are benign vascular growths seen in approximately 4% to 5% of infants.^{1,2} These lesions generally appear in the first few weeks of life, proliferate rapidly for 6 to 9 months, and then gradually involute.³ Most IH lesions regress over time without functional or cosmetic impairment, but a significant subset develop complications that can be life threatening or permanent.⁴

Potential complications of IH include impairment of visual or respiratory function, ulceration, permanent anatomic distortion, dyspigmentation, and significant scarring. Haggstrom and colleagues reported that 24% of 1,058 patients with IH who were followed in a national registry developed complications. The most common area of involvement is the face, with 22.9% of facial hemangiomas developing complications and 43% requiring intervention.⁴ The optimal approach to IH treatment consists of recognizing lesions that are more likely to be problematic based on location and rapidity of growth and intervening in a timely manner to prevent or minimize adverse sequelae.⁵ There is no standardized management strategy for IH, but a variety of treatments are used to decrease the proliferative phase and increase speed of involution.

These include corticosteroids, propranolol, laser therapy, and surgical excision.⁵ Early intervention with pulsed dye laser (PDL) is the focus of this article. Two of our patients received systemic therapy and localized PDL treatment, providing an “internal control” that documented the additive effects of combination therapy.

Methods and Description of Technique

We describe five patients who received early PDL for treatment of IH. The majority of these treatments were performed using oral acetaminophen and topical lidocaine for local anesthesia. The treatment parameters for each patient are outlined in Table 1. The affected areas were treated with nonoverlapping pulses using the 585- or 595-nm PDL (7- to 12-mm spot size, 5.0–10 J/cm², 0.45- to 1.5-ms pulse duration, and dynamic cooling spurt duration of 30 ms with 10- to 30-ms delay). The treatments were performed on an outpatient basis, and patients were discharged directly home with bacitracin ointment and ice packs. Repeat treatments were performed at approximately 2- to 8-week intervals until desired results were achieved and as needed subsequently in the case of recurrence.

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TABLE 1. Treatment Parameters

Case	Treatments, n	Interval Between Treatments, Weeks	Wavelength, nm	Energy Frequency, J/m ²	Pulse Width, mm	Spot Size, mm	Dynamic Cooling, ms Cryogen Spurt / ms Delay	Systemic Therapy	Other
1	6	4-8	585-595	5-6	0.45	10-12	30/30	Y	Orbital area not treated
2	8	2-12*	595	5-7.5	1.5	10	30/10	Y	
3	2	4	595	5.5-10	0.45-1.5	10-12	30/30	N	
4	2	10	595	10	0.45-1.5	7-10	30/30	Y	
5	8**	3-24***	595	7.5-8.5	1.5	7	30/10	Y	Patient with PHACES; orbital area not treated

*First six treatments were 2 weeks apart; two additional treatments were performed 3 months apart for slight rebound growth.

**Last three treatments for residual telangiectasias, parameters not included in above ranges.

***First four treatments performed 3-12 weeks apart, fourth treatment performed 6 months later because of rebound growth, last three treatments started 4 months later at 2-month intervals for residual telangiectasias.

Results

Case 1

Figure 1A shows a 1-month-old Caucasian girl with an extensive, proliferating, superficial segmental IH on the right frontotemporal scalp, right forehead, and eyelid before treatment. The patient received her first PDL treatment at 1 month of age. At this time, the orbital-periorbital area was not treated, given safety concerns regarding eyelid movement during the procedure. In coordination with the ophthalmology service, oral prednisone therapy was simultaneously initiated. One month after the first PDL treatment (Figure 1B), the areas exposed to PDL had dramatically improved, but the nontreated periorbital area continued to proliferate. The patient received five additional PDL treatments, and the hemangioma continued to involute. Six months after her final PDL treatment, a follow-up photograph at 13 months of age (Figure 1C) documented complete involution. No complications occurred.

Case 2

This 1-month old Caucasian girl had a 6- by 3-cm superficial, segmental, discontinuous, vascular, reticulated, red plaque on the left temporal maxillary region, tip of the nose, philtrum, and upper lip that developed shortly after birth. She received her first PDL treatment at 1 month and 3 days of life. Figure 2A shows her at 1 month and 24 days, after 1 month of prednisone and two PDL treatments.

She had six additional PDL treatments along with a 9-week course of prednisone and 6 months of propranolol. After discontinuing propranolol, she had slight rebound growth of the hemangioma that resolved after the final PDL treatment. A follow-up photograph (Figure 2B) taken at 10 months and 2 days of life (26 days after the final PDL treatment) shows near complete involution of the IH. She suffered no complications.

Case 3

Figure 3A shows a 1.5-month-old Caucasian girl with superficial IH characterized by a violaceous plaque on



Figure 1. (A) Pretreatment photograph demonstrates an extensive right frontotemporal scalp and facial lesion consistent with superficial segmental infantile hemangioma (IH). (B) One month after the first pulsed dye laser (PDL) treatment, the areas treated with PDL have dramatically improved, whereas the untreated area adjacent to the orbit continued to proliferate. (C) Six months after the sixth PDL treatment, a follow-up photograph revealed complete involution of the lesion.

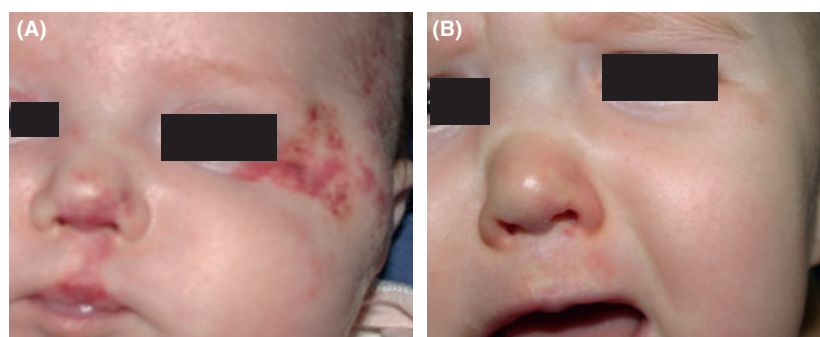


Figure 2. (A) Photograph after two pulsed dye laser (PDL) treatments demonstrates a superficial, segmental, interrupted, reticulated plaque circumscribing several blanching papules on the left temporal maxillary region, tip of the nose, philtrum, and upper lip. (B) After seven PDL treatments, a follow-up photograph revealed near-complete involution of the segmental infantile hemangioma (IH).

the right cheek. She had received no prior treatment for the lesion. She received her first PDL treatment at 1.5 months of age and the second at 3.5 months of age, resulting in excellent flattening and textural improvement of the lesion. Five months after the second laser treatment, at 8.5 months, a follow-up photograph (Figure 3B) shows that the lesion had almost completely involuted, and there is only residual skin erythema. No further treatment was required.

Case 4

Figure 4A shows a 3.5-month-old Caucasian boy with a previously untreated mixed IH. Physical examination revealed a left lower eyelid violaceous plaque. He received his first PDL treatment at 4.5 months of age, resulting in excellent flattening and textural surface improvement of the lesion. He

also received a 3-month course of prednisone. Two and a half months after the first PDL treatment, a follow-up photograph (Figure 4B) shows great improvement but not complete involution. The patient had an additional PDL treatment at this time. Six months after the second PDL treatment, the hemangioma had completely involuted. The patient suffered no complications.

Case 5

This 35-day-old Hispanic girl presented with a 6- by 4.5-cm violaceous plaque on the right face overlying the lateral one-third of the eyelid, temple, zygomatic arch, and temporal scalp consistent with mixed segmental IH. Magnetic resonance imaging and magnetic resonance angiography of the head and neck demonstrated an enhancing lesion in the right

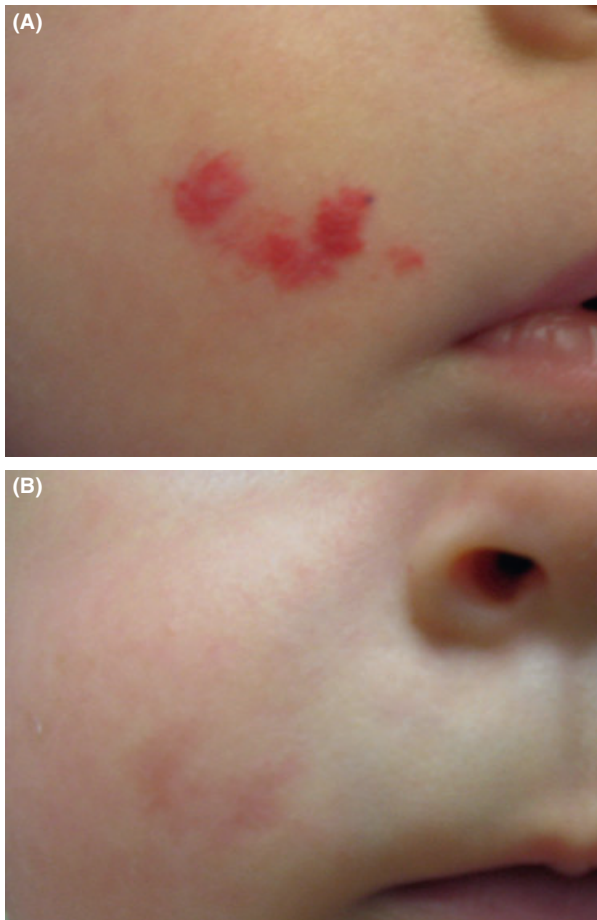


Figure 3. (A) Pretreatment photograph demonstrates right cheek violaceous plaque consistent with a superficial infantile hemangioma. (B) Five months after the second pulsed dye laser treatment, a follow-up photograph reveals near-complete involution of the hemangioma with residual skin erythema.

middle and posterior cranial fossae, a right preseptal hemangioma with mild proptosis of right globe, and an absent anterior cerebral artery. Ophthalmology consultation revealed an increased cup-to-disc ratio. Echocardiogram revealed total anomalous pulmonary venous return (TAPVR), large patent ductus arteriosus with left to right flow, and moderate right ventricular hypertrophy. Her presentation was consistent with PHACES syndrome (Posterior fossa malformations, Hemangiomas, Arterial anomalies, Cardiac defects, Eye abnormalities, and Sternal cleft/supraumbilical raphe). Cardiology initially recommended that oral corticosteroid therapy be deferred given her cardiopulmonary status secondary to TAPVR.

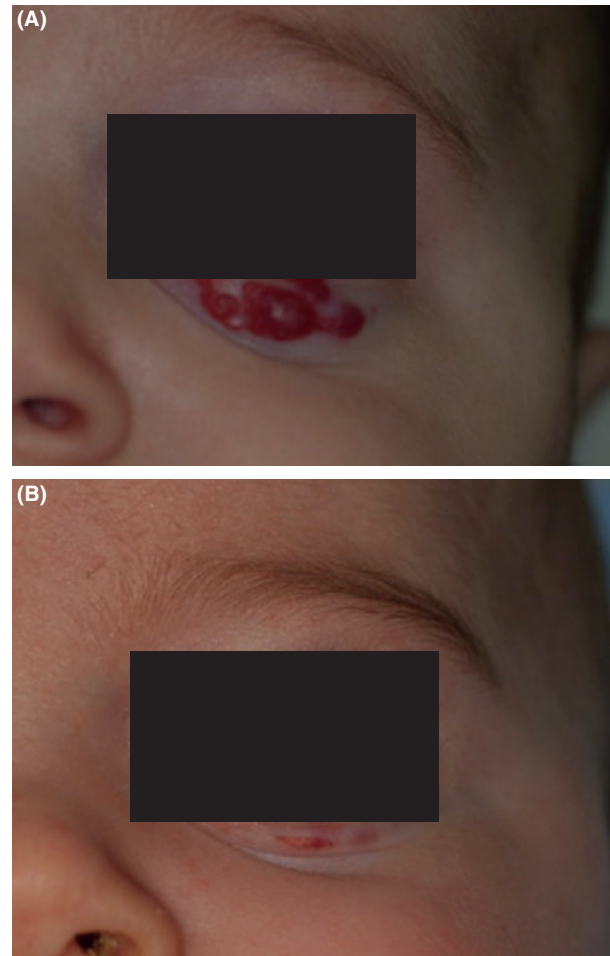


Figure 4. (A) Pretreatment photograph demonstrates a left lower eyelid violaceous plaque consistent with mixed infantile hemangioma. (B) Two and a half months after the first pulsed dye laser treatment, a follow-up photograph reveals great improvement in the lesion but not complete involution.

The patient received her first PDL treatment at 36 days of life. General anesthesia was deferred given concerns regarding her fragile cardiac status. The periorbital and orbital cutaneous surfaces were not treated because of motion of the lid and consequent safety concerns. The temporal and scalp area also received suboptimal therapy because of continuous motion of the child and concern for her cardiorespiratory status, as she became easily agitated and oxygen saturation dropped during the procedure. Three weeks after the first PDL treatment (Figure 5A), the treated areas began to stabilize or improve, with band-like areas of resolution that correlated with laser pulse sites, whereas the



Figure 5. (A) Photograph 3 weeks after the first pulsed dye laser (PDL) treatment demonstrates a mixed, violaceous, segmental plaque on the right face overlying the lateral one-third of the eyelid, temple, zygomatic arch, and temporal scalp, with band-like areas of clearing on the temple and scalp. (B) 6 weeks after the first PDL treatment, the untreated area overlying the orbit continued to proliferate. (C) After five PDL treatments, a follow-up photograph reveals soft tissue mass with residual segmental infantile hemangioma on the right face. Telangiectasias are more prominent and dense in the untreated area closer to the orbit.

untreated areas showed confluent proliferation that persisted over the next 3 weeks (Figure 5B). At 13 months of age, after completing a 6-month course of prednisone and five PDL treatments, a follow-up photograph (Figure 5C) reveals a 7- by 8-cm soft tissue mass with residual vascular telangiectasias for which the patient received three further PDL treatments.

Discussion

Most IH will spontaneously involute over time, and proliferation often clinically appears to have peaked on average at approximately 6 to 9 months of life. Regarding involution, the exact time course cannot be predicted, but some experts reference the “rule of tens,” such that approximately 30% will have involuted by age 3, 50% by age 5, 70% by age 7, and 90% by age 9. After spontaneous involution, 15% to 40% of patients can be left with residual skin changes, including pigmentary change, telangiectasias, and atrophy, as well as fibrofatty lesions that may need surgical correction.^{6,7} In our series of hemangiomas that received early PDL treatment, significant involution was seen by 8.5 to 13 months of age. Residual telangiectasias were subsequently removed with further PDL therapy.

Infantile hemangiomas can have a significant effect on the patient and his or her family, with physical

and psychosocial implications. The most common complications are ulceration and bleeding, occurring in 21% and 7.5% of patients, respectively.⁸ The rationale for treating is typically based on preventing functional impairment or decreasing pain, preventing or improving scarring and disfigurement, and avoiding life-threatening complications.⁵ The mainstay of treatment for decades was systemic corticosteroids, which are most effective during the proliferative phase.⁹ Another increasingly popular systemic treatment option is propranolol, which can be effective even after the proliferative phase is complete.¹⁰ In patients who have contraindications to systemic therapy or who have superficial IH responsive to topical or laser therapies, other treatment options include topical therapy with corticosteroids, imiquimod, timolol, intralesional therapy with corticosteroids, and PDL.⁵

Pulsed dye laser is a treatment option that allows for targeted results, especially in anatomically or cosmetically sensitive areas. Pulsed dye laser treatment can be effective in decreasing the proliferative phase of IH and increasing the rate of involution, with the added benefit of no systemic side effects.¹¹ The goal of laser treatment of hemangiomas is to maximize vascular damage while minimizing dermal and epidermal injury. Clinical improvement is measured according to clearance or improvement in color and decrease in thickness. Superficial hemangiomas show

a better clinical response than deep hemangiomas. The use of dynamic cooling provides epidermal protection, allowing more-effective fluences that can penetrate more deeply, as well as providing anesthetic relief. Even with dynamic cooling, the effect of PDL is limited to the most-superficial (1–1.3 mm) component of the lesion.¹¹ PDL does not treat the deep component of hemangiomas, and medical therapy is the treatment of choice for this component. The lesions of younger patients have been reported to respond more favorably than those of older patients, again emphasizing the need for early initiation of treatment.¹²

Side effects of PDL include ulceration, scarring, skin atrophy, and pigmentary changes, but the development of novel integrated cooling technology has decreased thermally induced epidermal damage and significantly decreased the rates of overall complications. A randomized controlled trial from 2002 comparing PDL with a wait-and-see policy reported greater skin atrophy and hypopigmentation in PDL patients, similar to residual scarring seen in naturally resolving lesions, but epidermal cooling was not used in this study.¹³ A more recent study involving 90 patients using epidermal cooling showed no scarring or atrophy, one patient with ulceration that resolved during treatment, hyperpigmentation in 4% of patients, and hypopigmentation in 14% of patients (16). This rate of residual skin changes is lower than for patients who undergo conservative management for IH.^{6,7} Laser treatment–related complications were not seen in any of the patients in our series.

Previous studies have shown that treating IH with PDL at 2-week intervals can help to decrease proliferation.^{11,14} Because of other medical problems or lack of adherence on the parents' part, treatment every 2 weeks is not always possible, and our series serves to show that beneficial effects of PDL can be seen with treatments spaced further apart. Experts have also shown that PDL with dynamic cooling using a 595-nm wavelength and pulse widths of up to 1.5 ms allows for deeper laser

penetration and excellent rates of clearance for superficial and mixed hemangiomas with minimal adverse effects.^{11,14} Because recent concerns have been raised that general anesthesia can affect cognitive development in children, parents may be hesitant to have children undergo general anesthesia for PDL treatment.¹⁵ It is often possible to treat a large surface area with PDL if an experienced doctor or nurse is present to stabilize the patient. With an experienced clinician and adequate monitoring, these treatments can be performed without general anesthesia. In Case 5 in our series, the patient had cardiopulmonary comorbidities that did not allow for general anesthesia but did not preclude PDL treatment. One of her treatments was terminated early because of respiratory compromise; however, she had several further treatments that she tolerated well.

Two of the patients in our series had hemangiomas extending to the orbit. In patients with orbital hemangiomas it is crucial to prevent obstruction of the visual access, which can lead to amblyopia. These patients require early initiation of medical therapy and should be followed by ophthalmology to monitor for development of visual complications. In our series, these orbital areas were not treated with PDL because of concern regarding eyelid motion and globe safety or parental refusal of general anesthesia. The orbital area in both of these patients continued to proliferate, whereas the treated areas proliferated less rapidly or began to regress. Although four of the patients in our series were also receiving systemic treatment, these two cases served as an internal control to show that early PDL treatment can decrease proliferation. Recently Hunzeker and Geronemus reported that early treatment using a 595-nm PDL can safely and effectively diminish proliferative growth and hasten resolution of superficial IH of the eyelid. They used metal corneal eye shields, which are available for placement in infants to protect the eyes and allow orbital PDL treatment, which can be performed in the office setting without general anesthesia.¹⁴

Four of the five patients in our series were receiving systemic therapy. In those receiving systemic therapy who had partial laser treatment, the treated sites responded faster than did the untreated sites. The use of systemic therapy should not preclude the use of PDL, which can be used as an adjunct to systemic therapy and alone. A recent unpublished study by Dr. Margitta Poetke of the Elisabeth Klinik in Berlin has shown the benefit of using propranolol in combination with pulsed laser therapy in the treatment of hemangiomas. At the Excellence in Paediatrics Annual Meeting in December 2010, Dr. Poetke reported a prospective, observational study of 23 patients ranging in age from 2 months to 3.5 years with large facial hemangiomas that were causing severe functional impairments. Seven of the patients had received prior oral corticosteroid therapy. Treatment was for 6 to 8 months, with 2 to 18 months of follow-up. Of 14 patients given propranolol in combination with laser therapy, only one experienced rebound hemangioma growth. Of nine patients treated with propranolol (2 mg/kg per day) alone, six had rebound growth when treatment was stopped. This study suggests that propranolol plus laser therapy may be more effective than propranolol alone and appears to be associated with the possibility of less rebound growth.

Early PDL treatment is a safe and effective option for selected patients with IH, including those who are undergoing systemic therapy. Pulsed dye laser alone can avoid the potential adverse side effects seen with systemic therapies or, when combined with systemic therapy, may provide an additional treatment strategy superior to monotherapy with a systemic agent. Although most IH do not require therapy, in appropriately selected cases, mono or adjuvant therapy with PDL can lead to more-rapid response and may decrease the risk of more-serious sequelae such as ulceration and disfigurement. Pulsed dye laser should be considered in appropriate patients and, when warranted, should be initiated as early as possible to maximize outcomes.

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