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Treatment of Port-Wine Stain Birthmarks Using the 1.5-msec Pulsed Dye Laser at High Fluences in Conjunction with Cryogen Spray Cooling

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BACKGROUND. The majority of port-wine stain (PWS) patients treated with the pulsed dye laser (PDL) do not achieve complete blanching. Safe administration of higher fluences has been proposed as a means of improving treatment efficacy.

OBJECTIVE. To determine the safety and efficacy of PWS treatment with the 1.5-msec PDL at high fluences in conjunction with cryogen spray cooling.

METHODS. Twenty PWS patients were treated with the PDL in combination with cryogen spray cooling utilizing a 7 or 10 mm spot size and fluences ranging from 6 to 15 J/cm². Before and after treatment photographs were compared on a blinded basis.

RESULTS. No scarring or skin textural changes occurred. Blanching scores were as follows: 20% of patients achieved 75% or greater blanching after an average of 3.3 treatments, 30% achieved 50–74% blanching, 20% achieved 25–49% blanching, and 30% achieved less than 25% blanching.

CONCLUSION. In conjunction with cryogen spray cooling, the PDL can be safely used at high fluences. At this time it is not clear that the use of higher fluences improves treatment efficacy; however, as other aspects of PWS laser treatment are optimized, safe administration of higher fluences is likely to be advantageous.

K.M. KELLY, MD, V.S. NANDA, MD, AND J.S. NELSON, MD, PHD HAVE INDICATED NO SIGNIFICANT INTEREST WITH COMMERCIAL SUPPORTERS.

PORT-WINE STAINS (PWSs) are congenital, vascular malformations of the skin found in approximately 0.3% of children.¹ PWSs may be located anywhere on the body, but are commonly found on the face and neck, where they may have serious psychological consequences.^{2–4} Patients are often perceived by others as “marked,” which may adversely affect personality development. Over time, these lesions may hypertrophy and patients may experience local bleeding. For these reasons, patients and their families often seek treatment.

Developing acceptable treatment options has been difficult. Early attempts included cosmetic cover-up, skin grafting, radiation, dermabrasion, cryosurgery, tattooing, and electrotherapy, but none of these modalities has provided cosmetically acceptable results. The development of lasers and their ability to selectively target PWS blood vessels offers an improved treatment option.^{5–7}

A variety of lasers have been utilized for the treatment of PWS birthmarks, but the pulsed dye laser

(PDL) has produced the best results with the lowest incidence of adverse effects. Yellow light emitted by the PDL is preferentially absorbed by hemoglobin, allowing more selective destruction of the ectatic capillaries in the dermis. However, the epidermis is not totally spared, due to partial absorption of energy by melanin, which presents an optical barrier through which light must pass to reach the underlying blood vessels.⁸ Absorption of laser energy by melanin causes localized heating in the epidermis, which may, if not controlled, produce permanent complications such as skin texture changes or dyspigmentation. Furthermore, epidermal melanin reduces the light dosage reaching the blood vessels, thereby decreasing the amount of heat produced in the targeted PWS and leading to sub-optimal blanching of the lesion. Unfortunately, for many lesions the threshold for epidermal damage following laser therapy is lower than that for permanent blanching of the PWS. Few patients obtain 100% fading of their PWS even after several treatments.^{9–11}

In recent years, scientists and clinicians have explored methods to improve treatment outcomes with PDL. The addition of epidermal cooling is one important innovation. Selective cooling of the epidermis allows the use of higher fluences, which is expected to result in greater photocoagulation of the targeted PWS vessels, while minimizing the risk of epidermal dam-

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age and adverse effects.¹²⁻¹⁷ Cryogen spray cooling is a safe and effective method for protecting the epidermis.

The traditional PDL uses a wavelength of 585 nm and a pulse duration of 450 msec. Alternative wavelengths and pulse durations have also been explored.¹⁸⁻²⁰ Theoretical predictions suggest that longer wavelengths should penetrate deeper into the dermis, while at the same time providing more uniform heating throughout larger vessels. Longer pulse widths may allow more effective treatment of larger blood vessels.

Currently there are lasers available that combine several of these proposed improvements, providing cryogen spray cooling in combination with a tunable PDL offering wavelengths of 585–600 nm and a pulse duration of 1.5 msec. The objective of this study was to determine the safety and efficacy of PWS treatment with a 1.5-msec PDL at high fluences in conjunction with cryogen spray cooling.

Methods

The research protocol was approved by the Institutional Review Board at the University of California, Irvine. Subjects were recruited from previously treated and untreated patients at the Beckman Laser Institute seeking removal of PWS birthmarks. Subjects gave written informed consent prior to their participation in the study. At each visit, documentation of the PWS was obtained by photographs. Attempts were made to take photographs under standardized conditions of magnification, lighting, angle, and film expo-

sure. Patients were clinically evaluated for adverse effects at each treatment visit.

Twenty patients were evaluated during the study. The ScleroPLUS® laser (Candela, Wayland, MA; $\tau_p = 1.5$ msec) was used to treat all patients. The U.S. Food and Drug Administration (FDA)-approved 1,1,1,2-tetrafluoroethane ($C_2H_2F_4$, BP = $-26.2^\circ C$) was used as the cryogen.²¹⁻²³ Cryogen spurt durations of 30–60 msec were utilized with delays of 10–30 msec between the coolant spray and the laser pulse. Most PWSs were treated with a 7 mm spot size and fluences ranging from 8 to 15 J/cm². PWSs of the neck and eyelids were treated with a 10 mm spot size and a fluence of 6 J/cm². Either a 585 or 595 nm wavelength was utilized. Treatments were repeated every 8–12 weeks.

Treatment and evaluation were continued for an 18-month study period or until a patient no longer desired further treatment. At the completion of the study, before and after treatment photographs were evaluated by three dermatologists not previously involved in the study who were blinded to treatment parameters.

Results

Twenty patients were enrolled and treated (Table 1). Subjects ranged in age from 2 months to 55 years (average 23 years). There were 14 females and 6 males (a ratio of 2.3:1). The distribution of Fitzpatrick skin types was as follows: type I, two patients; type II, seven patients; type III, four patients, and type IV, seven patients. All of the PWSs were on the face, neck,

Table 1. Patient and Treatment Characteristics

Patient no.	Age at first treatment (years)	Sex	PWS location	Previous treatment	Skin type	No. of treatments	Wavelength (nm)	Fluence ^a (J/cm ²)	Blanching (%)
1	23	F	Face/neck	Yes	III	3	595	9–12	50–74
2	14	F	Face	Yes	I	3	585, 595	8–14	<25
3	28	F	Face	No	II	5	585, 595	12–15	50–74
4	52	F	Upper lip	No	II	1	595	12	50–74
5	9	F	Face	No	IV	1	595	13.5	50–74
6	14	M	Face	Yes	IV	6	595	12	25–49
7	21	F	Face	No	II	4	585, 595	12–15	<25
8	9	M	Face	Yes	II	5	585, 595	9–15	<25
9	2 months	F	Face	No	III	1	595	10	50–74
10	35	M	Face	No	II	1	585	12	25–49
11	5	M	Face	No	IV	9	585, 595	7–15	25–49
12	3 years	F	Face	Yes	IV	4	585, 595	6–15	>75
13	2.5	M	Face	No	I	3	595	10–12	<25
14	48	M	Face/neck	No	II	4	595	10–12	50–74
15	13	F	Face	Yes	IV	4	585, 595	9–14	<25
16	13	F	Face	No	III	4	585, 595	12–15	<25
17	55	F	Face	No	II	3	595	12–15	>75
18	49	F	Lip	No	III	2	595	12–15	>75
19	39	F	Face/neck	No	IV	4	595	12–15	25–49
20	36	F	Lip	No	IV	4	585, 595	10–15	>75

^aLower fluences were used for the eyelids and neck.

or both. The number of treatments ranged from 1 to 9 (average 3.6).

None of the patients developed scarring. Two patients (10%) with type IV skin developed hyperpigmentation. Twenty percent of patients achieved more than 75% blanching after an average of 3.3 treatments (Table 1). Near-complete blanching was achieved in two adult patients with PWSs of the upper lip (Figure 1) and face (Figure 2). Another adult patient with a thickened PWS of the temple achieved an excellent result (Figure 3). Thirty percent of patients were evaluated to have blanching of 50–74%, 20% had blanching of 25–49%, and 30% had less than 25% blanching.

Discussion

This study clearly demonstrates that treatment of PWS with PDL in conjunction with cryogen spray cooling is safe at high incident light doses. No patients experienced scarring after the more than 70 treatments included in this evaluation. Two patients with type IV skin developed hyperpigmentation. At this time, these patients are still undergoing treatment of their PWSs approximately every 8 weeks and thus the hyperpigmentation has not had time to resolve. However, in our experience, this dyspigmentation is likely to improve or resolve completely with time.

Reyes and Geronemus²⁴ evaluated 73 patients undergoing PWS treatment using a PDL at lower fluences (5.5–8 J/cm²) without cryogen spray cooling and reported the following study outcomes: cutaneous depressions in 5%, hyperpigmentation in 22%, and hypopigmentation in 4%. While our evaluation includes a smaller number of patients, our results seem to indicate that the PDL in conjunction with cryogen spray cooling has an excellent safety profile and is associated with fewer adverse effects than PDL without cryogen spray cooling used at significantly lower fluences. The safety of PDL in conjunction with cryogen spray cooling is largely a result of the effective epidermal protection provided by the cryogen. When a 1-msec cryogen spurt is applied to the skin surface, the cooling remains localized to the epidermis while leaving the temperature of targeted dermal structures unchanged

Figure 2. A 37-year-old man with PWS of his face A) prior to laser treatment, and B) after three treatments with PDL.

and therefore susceptible to laser thermal injury. As a result, cryogen spray cooling effectively increases the threshold for epidermal damage, allowing the use of higher fluences, even in patients with darker skin types.

It is more difficult to determine if the use of this laser at high fluences results in improved efficacy. Because we determined that the addition of cryogen spray cooling improved safety, all of our patients with PWS have been treated with PDL in conjunction with cryogen spray cooling with few exceptions since 1999. Thus we must rely on previously published reports to compare our efficacy results with those obtained using earlier PDL models. In 1990, Reyes and Geronemus²⁴ evaluated 73 patients with 76 PWSs after treatment with PDL without cryogen spray cooling and determined that 45% achieved more than 75% lightening after an average of 2.5 treatments. All of their patients were less than 14 years of age (average 6 years 2 months). The distribution of Fitzpatrick skin types was not reported.

Geronemus²⁵ recently reported more than 75% clearing after an average of four treatments in 63% of 16 infants treated with the same laser used in our study using fluences of 11–12 J/cm². The distribution of Fitzpatrick skin types was not reported.

A smaller percentage of our patients (20%) achieved more than 75% blanching after an average of 3.3 treatments. We believe our results offer a realistic assessment of achievable therapeutic efficacy with current technology over a broad range of patients. Three aspects of our study population are important to note in regards to assessment of treatment efficacy. Only one of our patients was an infant. In general, our patients were significantly older (average age 23 years) than those in-

Figure 1. A 49-year-old woman with PWS of her lip A) prior to laser treatment, and B) after two treatments with PDL.

Figure 3. A 55-year-old woman with PWS of her face A) prior to laser treatment, and B) after three treatments with PDL.

cluded in previous studies. Many believe that PWSs are generally easier to treat in younger patients,^{24,26} however, this opinion is somewhat controversial.²⁷

Second, we included in this study many patients (55%) with darker skin types. Absorption of laser energy by melanin inhibits light delivery to the targeted PWS vessels, and thus darker skin types are generally more difficult to treat and more susceptible to adverse effects.

Third, we also included in this study several patients with resistant PWSs that had limited response to either the traditional PDL without cryogen spray cooling or the potassium titanyl phosphate (KTP) laser. Several characteristics that affect PWS treatment outcome have been identified, including lesion location, patient age, and skin type.^{26,28} However, some patients do not achieve good results after many laser treatments, even though there are no identifiable factors that would predict poor outcome. It is likely that the vessels of these PWSs are larger and deeper. Currently there is no noninvasive imaging method to identify these patients; however, in our laboratories we are exploring imaging methods, such as infrared tomography and optical Doppler tomography, which may help predict treatment prognosis in the future.^{29,30}

We believe that higher fluences will ultimately increase treatment efficacy, but clearly other factors must also be optimized to achieve consistent and significant PWS blanching in all patients. We are evaluating the role of wavelength, pulse duration, and cryogen spray cooling parameters. In addition, we are working to develop methods for rapidly measuring epidermal melanin concentration and the size and depth of vessels in PWSs in an effort to optimize treatment parameters on an individual patient basis.³⁰

We have also treated hemangiomas with PDL in conjunction with cryogen spray cooling. Because hemangiomas generally regress on their own with time, laser treatment of these lesions is more controversial and generally reserved for lesions that are rapidly growing, problematic because of ulceration, bleeding, or secondary infection, or impinging on vital structures such as the eyes or nose. We treated six children with hemangiomas that met these criteria. All patients achieved stabilization and subsequent regression of their lesions. Two patients developed atrophic scars. We believe that these were a result of rapid enlargement and then regression of the lesions and not an adverse effect associated with laser use; however, this latter possibility cannot be ruled out. Of course, it is not entirely clear whether improvement of these lesions occurred because of successful laser intervention or a natural involution of the lesions. However, we believe that PDL in conjunction with cryogen spray cooling may also have a role in the treatment of carefully selected patients with hemangiomas.

Conclusion

In summary, we have demonstrated that PDL using high fluences in conjunction with cryogen spray cooling is safe. At this time it is unclear that the use of higher fluences improves treatment efficacy. However, as other aspects of PWS laser treatment, including wavelength, pulse duration, and cryogen parameters, are optimized, it is likely that safe administration of higher fluences is likely to be advantageous.

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