

## ORIGINAL ARTICLE

# Investigation into optimal treatment intervals of facial port-wine stains using the pulsed dye laser

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**Background:** Port-wine stains (PWS) affect 0.3% to 0.5% of newborns and pulsed dye laser (PDL) remains the treatment of choice. Optimal treatment intervals have not been established.

**Objective:** We sought to validate the optimal treatment intervals for the management of facial PWS with PDL.

**Methods:** In all, 24 infants with facial PWS who received at least 5 treatments with the PDL at 2-, 3-, and 4-week intervals at a private laser and skin surgery center from 2009 to 2010 were identified by a retrospective chart review. Safety and efficacy were compared by blinded investigators.

**Results:** Side effects were equivalent in all interval groups and included only expected short-term erythema, edema, purpura, and mild postinflammatory hyperpigmentation. No patient developed hypopigmentation, scarring, or infection. All interval groups showed 50% to 100% clearance of their PWS after 5 treatments. Complete or near-complete clearance was seen in 6 of 8 (75%) and 7 of 8 (87.5%) patients in the 2- and 3-week interval groups, respectively, as compared with 3 of 8 (37.5%) patients in the 4-week interval group.

**Limitations:** This was a retrospective chart review from a single institution. Long-term side effects and recurrence rates were not assessed.

**Conclusion:** We conclude that PDL treatments at 2-, 3-, and 4-week intervals are effective for the management of facial PWS in infants with minimal short-term side effects. Shorter treatment intervals may allow for relatively more rapid and more effective treatment. (J Am Acad Dermatol 10.1016/j.jaad.2011.11.964.)

**Key words:** capillary vascular malformation; laser therapy; vascular birthmarks.

Port-wine stains (PWS) are congenital low-flow vascular malformations that occur in approximately 0.3% to 0.5% of newborns.<sup>1</sup> Most lesions occur in the head and neck area.<sup>2</sup> Over 40% of PWS are anatomically restricted to the cutaneous distribution of the trigeminal nerve. The natural history of PWS without intervention is to darken and thicken over time with an estimated 65% developing hypertrophy and nodularity by the fifth decade.<sup>3</sup> With the development of hypertrophy, the risk of spontaneous bleeding and pyogenic granuloma

formation also increases.<sup>4</sup> In addition to the medical complications, persons with PWS experience a considerable degree of psychological morbidity.<sup>5,6</sup>

The flash lamp pulsed dye laser (PDL) was the first laser specifically designed for cutaneous vascular lesions using principles of selective photothermolysis.<sup>7</sup> It has since become the gold standard for treatment of PWS.

Many factors influence the efficacy of laser treatment such as lesion size,<sup>8,9</sup> color,<sup>10,11</sup> localization,<sup>10</sup> hypertrophy,<sup>12</sup> or vessel architecture.<sup>13</sup> Lesions

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located on the periorbital area, lateral facial cheeks, chest, and proximal aspect of the arms respond best to treatment, whereas the malar areas of the face and distal limbs do not respond as well.<sup>14</sup> In addition, early age of treatment onset has been shown to improve response to treatment<sup>15</sup> and lower long-term relapse rates.<sup>16</sup> Despite appreciation for these influencing factors, optimal treatment intervals have not yet been defined.

The purpose of this study was to assess the relative safety and efficacy of PDL treatments at 2-, 3-, and 4-week intervals in patients with facial PWS.

## METHODS

### Patients

This was a retrospective chart review of patients with facial PWS at a private laser and skin surgery center from 2009 to 2010. Institutional review board approval was obtained for the study. A total of 24 patients were randomly selected by including the first 8 patients with facial PWS found to have been treated at 2-, 3-, and 4-week intervals on review of charts in reverse chronological order. Patients were included if they received at least 5 PDL treatments starting in infancy, defined as younger than 1 year of age. Patients were excluded if more than one of their 5 consecutive treatments diverged by more than 2 days from the intended treatment interval. Information on age, sex, anatomic location, side effects, and adverse events was obtained from chart records. Efficacy was assessed by comparison of photographs before and after 5 treatment sessions by blinded staff dermatologists, and graded based on percentage improvement with the following intervals: 0% (no improvement), 1% to 25% (mild improvement), 26% to 50% (moderate improvement), 51% to 75% (marked improvement); 76% to 95% (near total clearance), 96% to 100% (clearance).

### Laser

All treatments were performed using the 595-nm V-beam PDL (Candela Corp, Wayland, MA). Fluence settings ranged from 8.5 to 9.5 J/cm<sup>2</sup>, with a 10-mm spot size and 1.5-millisecond pulse duration. Dynamic cooling was used with a tetrafluoroethane spray 30 milliseconds before each laser pulse followed by a 20-millisecond postlaser pulse delay. For

treatment, patients were immobilized by nurses and their eyes protected by metal intraocular shields, externally applied aluminum-plated goggles, or multiple layers of gauze depending on the lesion proximity to the eyes. No anesthesia was used. Pulses were delivered to the entire lesion, overlapping no more than 10%. A cool hydrogel dressing was applied

immediately posttreatment for a few minutes but further wound care was not required. Photographs were taken of all patients before each treatment by nurses trained in dermatologic photography using digital cameras under similar lighting conditions.

### Statistical analysis

Differences in age between the treatment groups were evaluated by analysis of variance. The nonparametric Mann-Whitney U test or Wilcoxon rank sum test was used to assess the effect of treatment interval on lesion clearance.

## CAPSULE SUMMARY

- Optimal treatment intervals have not been established for pulsed dye laser treatment of facial port-wine stains.
- Our experience is that pulsed dye laser treatment at 2-, 3-, and 4-week intervals is effective for infants with facial port-wine stains with minimal short-term side effects. Shorter treatment intervals may allow for relatively more rapid improvement.
- Practitioners treating port-wine stains may wish to consider these findings when establishing pulsed dye laser treatment protocols.

## RESULTS

### Demographics and patient characteristics

A retrospective record review identified 24 infants who presented to our office between 2009 and 2010 for treatment of facial PWS and who met selection criteria. Clinical characteristics of selected patients including age, gender, and lesion location did not differ by interval arm (Table I). The average age at first treatment was 5.25 weeks (range 1-16), 4.25 weeks (range 1-16), and 7.38 weeks (range 2-16) in the 2-, 3-, and 4-week interval groups, respectively ( $P = .498$ ). Gender was similar across all groups with girls representing 50% of the 2-week interval population and 62.5% of the 3- and 4-week interval populations. All patients had Fitzpatrick skin types I through III and there was no significant difference in skin type between treatment groups (data not shown). All lesions included for analysis were located on the face; however, some patients had additional PWS outside this area that are also included in Table I.

### Safety

Overall, laser treatments were well tolerated and low rates of short-term side effects were equivalent among all interval groups. These effects included erythema, edema, and purpura. In addition, mild transient postinflammatory hyperpigmentation was

**Table I.** Pulsed dye laser treatment of port-wine stains in 24 infants: demographics and clinical characteristics

	Gender	Age at first treatment, wk	Location of lesion	Extrafacial lesion location	Erythema	Purpura	Edema	PIH	Percent improvement
2-wk Treatment intervals	F	2	Bilateral V1, V2, V3		X	X	X		51-75
	F	16	V1, V2, V3		X	X	X		76-95
	M	3	V2		X	X	X		51-75
	M	1	V1, V2		X	X	X	X	96-100
	F	10	V2		X	X	X		96-100
	M	1	V1		X	X	X		76-95
	M	8	Centrofacial	Leg	X	X	X		76-95
	F	1	Bilateral V1, V2, V3	Back	X	X	X		96-100
3-wk Treatment intervals	F	3	V1,V3	Chest, arm	X	X	X		51-75
	F	1	V3	Neck	X	X	X		76-95
	M	1	V2		X	X	X	X	96-100
	F	3	V2		X	X	X		96-100
	F	1	V1		X	X	X		96-100
	M	5	V2		X	X	X		76-95
	F	16	V2	Neck, back	X	X	X		76-95
4-wk Treatment intervals	M	4	V3		X	X	X		76-95
	F	16	V2		X	X	X		51-75
	F	2	Periorbital, temple		X	X	X		76-95
	F	3	V1, V2	Back, leg	X	X	X		51-75
	F	2	V1		X	X	X	X	96-100
	M	12	V2		X	X	X		51-75
	M	4	V2		X	X	X		51-75
	M	8	Periorbital		X	X	X		51-75
F	12	Centrofacial		X	X	X		76-95	

F, Female; M, male; PIH, transient postinflammatory hyperpigmentation; V1, ophthalmic branch of trigeminal nerve; V2, maxillary branch of trigeminal nerve; V3, mandibular branch of trigeminal nerve.

seen in one of 8 patients in all 3 interval groups. No unexpected or long-term adverse events including scarring, hypopigmentation, or infection were found in any interval group.

### Efficacy

All interval groups showed 50% to 100% improvement in the clinical appearance of the PWS after 5 treatments. A representative example of clinical response is shown in Fig 1. Complete clearance (96%-100%) was seen in 3 of 8 patients (37.5%) in the 2-week group, 3 of 8 patients (37.5%) in the 3-week group, and 1 of 8 patients (12.5%) in the 4-week group. Near-complete clearance (76%-95%) was seen in 3 of 8 patients (37.5%) in the 2-week group, 4 of 8 patients (50%) in the 3-week group, and 2 of 8 patients (25%) in the 4-week group. Moderate improvement (51%-75%) was seen in 2 of 8 patients (25%) in the 2-week group, 1 of 8 patients (12.5%) in the 3-week group, and 5 of 8 patients (62.5%) in the 4-week group. None of the patients experienced no improvement (0%) or mild improvement (1%-25%) at any treatment interval. These results are shown in

Fig 2. A trend towards a significant difference in efficacy was observed between 3- versus 4-week intervals ( $P = .074$ ), but no trend or statistical difference was observed when comparing 2-week intervals with 3-week ( $P = .79$ ) or 4-week ( $P = .16$ ) intervals.

### DISCUSSION

Several prior studies have validated the benefits of early intervention with PDL for the management of PWS. Our group previously validated the safety of the use of PDL in infants as young as 6 weeks.<sup>17</sup> Reyes et al<sup>18</sup> evaluated 73 patients and found that patients aged 3 months to 6 years showed 55% mean lightening after one PDL treatment, whereas children older than 7 years showed 48% mean lightening. In a retrospective study of 133 patients, 89.4% and 90% of patients with PWS aged 0 to 5 and 6 to 10 years, respectively, had good or excellent responses as compared with 66.7% of those older than 50 years.<sup>19</sup> Another study of 83 patients between the ages of 2 weeks and 17 years systematically investigated the effect of laser treatment based on the age of the

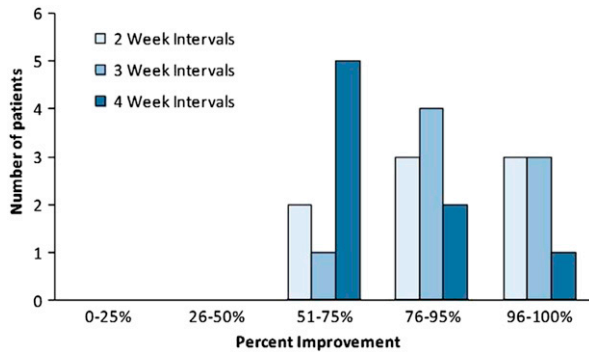


**Fig 1.** Clinical photographs of selected patients with facial port-wine stains demonstrating 96% to 100% clearance after 5 treatments at 2-, 3-, and 4-week intervals. Before and after treatment photographs of patients at 2-week (**A** and **B**), 3-week (**C** and **D**), and 4-week (**E** and **F**) treatment intervals. **D**, Postinflammatory hyperpigmentation.

patient and concluded that the rate of clearing decreases with increasing age at initial treatment. This study showed that 32% of patients before 1 year of age had complete clearance of their PWS, as measured by improvement in lesion size, compared with 18% of patients older than 1 year.<sup>8</sup> In a study investigating treatment efficacy as a function of patient age and number of treatment sessions of 91 facial PWS treated with PDL, patients younger than 1 year showed a decrease in size by 63% after the first 5 treatments and 33% after the second 5; if 1 to 6 years old, PWS decreased by 48% and 15% after each 5 treatment sessions; if older than 6 years, PWS decreased by 54% and 10% after each 5 treatment sessions.<sup>9</sup> Finally, in another study by our group, 49 infants younger than 6 months of age were treated with PDL at 4- to 6-week treatment intervals with

average clearance rates of 88.6% and no long-term adverse events.<sup>15</sup>

There are many potential advantages of more frequent treatment intervals for infants with PWS. First, shorter treatment intervals capitalize on the therapeutic benefit of early treatment by maximizing the number of sessions in this more responsive period. Moreover, maximizing therapy in infancy is logistically simpler. Lesions are smaller and therefore treatments are quicker. In addition, patients can be held still easily without general anesthesia, preventing the need for costly and time-consuming hospital-based operating room therapy. Shorter treatment intervals can also shorten the overall treatment period necessary to achieve complete or near total clearance. This improves the chance of erasing evidence of the PWS before early childhood and



**Fig 2.** Number of patients with facial port-wine stains grouped by percentage improvement after 5 pulsed dye laser sessions and by treatment intervals.

therefore eliminating the psychological burden that comes with awareness and taunting in preschool and school ages. In a survey of 259 patients and their families who were either undergoing PDL treatment for PWS or on the waiting list to start treatment, 75% considered that PWS negatively impacted their lives and 62% were convinced that their lives would change radically if the PWS could be eliminated. Comparing the pretreatment and posttreatment groups for children younger than 9 years, family members responded that 51% had problems in school and 27% had behavioral outbursts before treatment compared with 3% and 0% after treatment.<sup>20</sup>

Despite the theoretical advantages of more frequent treatment intervals, there are currently limited data to support its widespread implementation. Few studies have investigated the effect of treatment intervals in the management of PWS with PDL. A survey of 45 members of the British Skin Laser Study Group revealed that 84% of respondents considered 2 to 3 months as the optimal interval for PDL treatments.<sup>21</sup> A prospective split-lesion study of 16 PWS compared the effect of two treatment sessions, one half receiving the sessions 2 weeks apart and the other half 6 weeks apart. Blinded physician assessment and objective reflectance spectrophotometer measurements endorsed a 2-week treatment interval while no adverse events were recorded in either group.<sup>22</sup>

Similar to other retrospective reviews, the major limitation of our study includes the absence of rigorous controls for patients assigned to the various treatment arms. We only included patients with facial PWS and our results cannot be generalized to other anatomic locations. Furthermore, clearance rates were determined by subjective assessments of clinical photographs instead of more quantitative measures of lesion color. In addition, we present an

overall short follow-up time with data analyzed only until completion of the fifth treatment; therefore, we were unable to assess the effect of treatment interval on recurrence rates. Rates of recurrence after PDL treatment of PWS have been reported to be 11% to 50% in various reports.<sup>2,23,24</sup> Michel et al<sup>16</sup> showed that recurrence rates are correlated with age at first treatment with 0% of patients who initiated treatment before 1 year of age showing relapse after more than 1 year. We do not anticipate high recurrence rates in our study population but addition of these data would further validate the strategy of “treat early and treat often.” Given the benefits of early intervention as discussed previously and the potential advantages to more frequent treatment intervals as shown in the current study, additional studies with longer follow-up are warranted to further characterize the effects of these intervals on long-term side effects and recurrence rates.

In conclusion, our results confirm the safety of PDL treatments at 2-, 3-, and 4-week intervals for the management of facial PWS in infants. Moreover, in our study, shorter treatment intervals favored a better response after the same number of treatments, although not reaching statistical significance. We believe that even if results are equivalent in all groups after the same number of treatments, achievement of those results in a shorter time frame offers invaluable medical and psychological benefits for our patients.

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