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Prospective Study of Port Wine Stain Treatment With Dye Laser: Comparison of Two Wavelengths (585 nm vs. 595 nm) and Two Pulse Durations (0.5 Milliseconds vs. 20 Milliseconds)

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Background and Objectives: The conventional pulsed-dye laser (wavelength 585 nm, pulse duration 0.5 milliseconds) is seen as the standard treatment for port wine stains (PWS). Using the pulsed-dye laser at wavelengths of 590, 595, and 600 nm and at varying pulse durations of 1.5–40 milliseconds is one of the newest developments in the field, the therapeutic value of which has been examined in only a few studies. Treatment of PWS with short- and long-pulse dye lasers. Comparison of two wavelengths (585 nm vs. 595 nm) and two pulse durations (0.5 milliseconds vs. 20 milliseconds).
Study Design/Materials and Methods: Fifteen patients with untreated PWS were included in a randomized prospective study with three different laser settings. Patients underwent one treatment session. The following treatment parameters were chosen at a uniform spot size of 7 mm: (1) 585 nm/0.5 milliseconds/5.5 J/cm^2, (2) 595 nm/0.5 milliseconds/5.5 J/cm^2, and (3) 595 nm/20 milliseconds/13 J/cm^2. The clearance as well as side effects was evaluated. All treatments were performed with cold air-cooling. Follow-up took place immediately, 2 days and 4 weeks after the treatment. The PWS was assigned a clearance score (CS) from 1 to 4 (1 = poor to 4 = excellent).
Results: Descriptively, 585 nm/0.5 milliseconds generated the best average CS of 2.7, followed by 595 nm/20 milliseconds (2.5) and 595 nm/0.5 milliseconds (1.6)); statistically, there is no difference between the CS of 585 nm/0.5 milliseconds and 595 nm/20 milliseconds. The best lightening rates overall were achieved in purple PWS (CS = 3.5) versus red (CS = 2.5) and pink (CS = 2.0). Purple PWS responded best to 585 nm/0.5 milliseconds; red and pink PWS yielded similar results with 585 nm/0.5 milliseconds and 595 nm/20 milliseconds. The setting, 595 nm/0.5 milliseconds was clearly not as effective as the other laser settings. Purpura, pain, and crusting were most commonly reported after treatments with 585 nm/0.5 milliseconds (93%/93%/33%), closely followed by treatments at 595 nm/20 milliseconds (86%/93%/20%). The settings 595 nm/0.5 milliseconds yielded the lowest rate of adverse effects (67%/60%/0%). Hypopigmentation only occurred in one case (585 nm/0.5 milliseconds), and there were no reports of hyperpigmentation or scarring.
Conclusions: With respect to treating PWS, the conventional pulsed-dye laser set to 585 nm/0.5 milliseconds yields a significantly greater clearance rate than it does at a setting of 595 nm (with the same pulse duration, fluence, and spot size), although the former also entails the highest spectrum of adverse effects. In this study, purple PWS treated at these parameters showed the best results. In dealing with pink PWS, the results were similar to those of the conventional pulsed-dye laser when the pulse duration was increased to 20 milliseconds and fluence was increased. As a rule, the clearance rate corresponded to the extent of the postoperative purpura. Lasers Surg. Med. 34:168–173, 2004. © 2004 Wiley-Liss, Inc.

Key words: port wine stain; dye laser; long pulse; pulse duration; wavelength

INTRODUCTION

The pulsed-dye laser, set to a wavelength of 585 nm and a pulse duration of 0.5 milliseconds, has been a standard treatment of port wine stains (PWS) since as early as the 1980s. PWS response to laser treatment depends upon various factors (age, localization, size, color) and cannot generally be predicted [1–7]. After an average of four to eight sessions, PWS lighten by over 75% in around 40% of the patients. A clearance rate of below 50% has been described in literature in approximately 14–40% of all cases [3,8,9].

The development of pulsed-dye lasers with differing wavelengths and pulse durations was the outcome of largely experimental studies and theoretical models in which attempts were made to explain and determine why vascular skin changes were not responding to the conventional pulsed-dye laser (585 nm, 0.5 milliseconds) [10–12]. In the meantime, pulsed-dye lasers are available at wavelengths of 585–600 nm, pulse durations of up to 40 milliseconds and

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much higher fluences. A clinical assessment of these new devices has yet to keep up with their increasingly widespread use, however, and there are only few studies on the topic [13–17]. Edström and Ros focused on a comparison of 585 and 600 nm; Chang et al. assessed the wavelengths 585 and 595 nm with a pulse duration of 1.5 milliseconds each in conjunction with cryogen-spray cooling in their retrospective study. Scherer et al. examined different wavelengths (585, 590, 595, 600 nm), pulse durations (0.5, 1.5 milliseconds) and applied different spot sizes; Bencini evaluated a multilayer technique (two passes) on four patients; and Lou and Geronemus tested different fluences and pulse durations of a 595-nm pulsed-dye laser on two patients.

In this study, we focused on five questions: [1] What effects do wavelengths of 585 nm versus 595 nm have on the clearance of PWS when the pulse and fluence remain constant? [2] Which differences are there in the effects of varying laser settings have on pink, red, and purple PWS? [3] When pulse duration and fluence are increased, what effect does a wavelength of 595 nm have on clearance in comparison with the conventional pulsed-dye laser? [4] How do differing laser settings affect the spectrum of adverse effects? [5] Is there a correlation between post-operative purpura and the clearance rate?

TABLE 1. Demographic Data

Sex	
Female	10 (66%)
Male	5 (34%)
Age	
Range	11–44
Mean age	26
Fitzpatrick's skin type	
I	2 (13%)
II	12 (80%)
III	1 (7%)
IV–VI	—
Localization	
Face and neck	11 (73%)
Arm, shoulder	1 (7%)
Leg	2 (13%)
Back	1 (7%)
Size	
<10 cm^2	4 (27%)
10–100 cm^2	9 (60%)
>100 cm^2	2 (13%)
Color	
Purple	4 (27%)
Red	7 (46%)
Pink	4 (27%)

PATIENTS AND METHODS

Fifteen patients (10 female and 5 male) with untreated PWS were included in a randomized prospective study between 02/2001 and 02/2002. For forensic reasons, only untanned patients or patients with Fitzpatrick skin types I–III were evaluated.

The mean patient age was 26 with a range from 11 to 44 years. Seventy-three percent of the PWS were located on the head, 7% on the arm and shoulder, 13% on the leg, and 7% on the back. The classification of Fitzpatrick skin types was as follows: Type I: 2 (13%), Type II: 12 (80%), Type III: 1 (7%). Four (27%) of the PWS were <10 cm^2, 9 (60%) were 10–100 cm^2, and 2 (13%) were > 100 cm^2. Four (27%) had a purple, 7 (46%) a red, and 4 (27%) a pink PWS (Table 1).

Either the entire area or a sample area (10 × 10 cm^2) of the PWS was treated. The pulsed-dye lasers Photogenica V (Cynosure, Chelmsfort, CA, $\lambda = 585$ nm, $\tau_p = 450$ microseconds) and V-Star (Cynosure, Chelmsfort, CA, $\lambda =$ 595 nm, $\tau_p = 450$ microseconds to 40 milliseconds) combined with the cooling device Cryo 5 (Zimmer, Ulm, Germany) were used.

The following treatment parameters were chosen at a uniform spot size of 7 mm: Area 1: 585 nm, 0.5 milliseconds, 5.5 J/cm^2; Area 2: 595 nm, 0.5 milliseconds, 5.5 J/cm^2; Area 3: 595 nm, 20 milliseconds, 13 J/cm^2. Treatment was always performed at cooling level 5.

Based on comparisons between pre- and post-treatment photographs, each patient's PWS was assigned a clearance score (CS) of poor (1, <25%), fair (2, 26–50%), good (3, 51–75%), or excellent (4, 76–100%). The clearance was evaluated 4 weeks after the treatment by three independent physicians who were not otherwise involved in the study.

Concomitant side effects (intraoperative pain, purpura) were evaluated immediately (pain) and 2 hours (purpura) after the treatment; adverse side effects (crusting, hypo-/hyperpigmentation, scarring) were assessed after 2 days and 4 weeks. Pain was evaluated by the patients themselves, and all other parameters by three independent physicians. The classifications were as follows: + (clearly defined), +/− (weakly defined), and − (not present). Finer distinctions were made only for quantifying the purpura: +++ (very strong), ++ (strong), + (weak), − (not present).

Photos were taken with a Canon EOS100, using Agfa Ctx100 film. All patients gave their written consent.

RESULTS

Altogether, the results of 15 patients were assessed. Descriptively, the wavelength of 585 nm and a pulse duration of 0.5 milliseconds brought about the best results with an average CS of 2.7 (Fig. 1A/B), followed by 595 nm/20 milliseconds (CS = 2.1) and 595 nm/0.5 milliseconds (CS = 1.6) (Table 2); statistically, there is no difference between the CS of 585 nm/0.5 milliseconds and 595 nm/20 milliseconds.

Purple PWS showed the greatest overall response to pulsed-dye laser treatment (CS = 3.5); red PWS rated a CS of 2.5 (Fig. 2A,B), and pink a CS of 2.0. The best results were observed with the conventional pulsed-dye laser (585 nm, 0.5 milliseconds) on purple PWS; in dealing with red and pink PWS, comparable lightening rates were observed at parameters of 585 nm/0.5 milliseconds and 595 nm/20 milliseconds. A wavelength of 595 nm with a concurrent increase of the pulse duration (20 milliseconds) and of the

Fig. 1. **A**: PWS before treatment. **B**: Four weeks after the treatment. **Right side**: 585 nm/0.5 milliseconds (CS = 4), **middle**: 595 nm/0.5 milliseconds (CS = 1), **left side**: 595 nm/20 milliseconds (CS = 3). [Figure can be viewed in color online via www.interscience.wiley.com.]

fluence (13 J/cm^2) showed much greater efficacy than 595 nm/0.5 milliseconds (Table 3).

Postoperative purpura was darkest after treatment at 585 nm/0.5 milliseconds (93% of patients), followed by 595 nm/20 milliseconds (86%) and 595 nm/0.5 milliseconds (67%). The extent of the purpura in different groups is depicted in Table 4. The best CS (2.7) was noted in the group treated at 585 nm/0.5 milliseconds, which had very strongly defined purpura, followed by the group with parameters of 595 nm/20 milliseconds and strongly defined purpura (CS = 2.5). One patient did not develop purpura at any of the settings and still had a CS of 4 when treated at 585 nm/0.5 milliseconds and a CS of 2 for both of the other parameters.

When the parameters were set to 585 nm/0.5 milliseconds, pain and crusting were most common and most clearly marked (93%/33%). These adverse effects were reported less frequently in the group treated at 595 nm/20 milliseconds (93%/20%). The lowest rate of adverse effects occurred when patients were treated at 595 nm/0.5 milliseconds; here only 60% had pain, and there was no crusting at all. Hypopigmentation only occurred in one instance (585 nm/0.5 milliseconds); hyperpigmentation and scarring were not observed (Table 5).

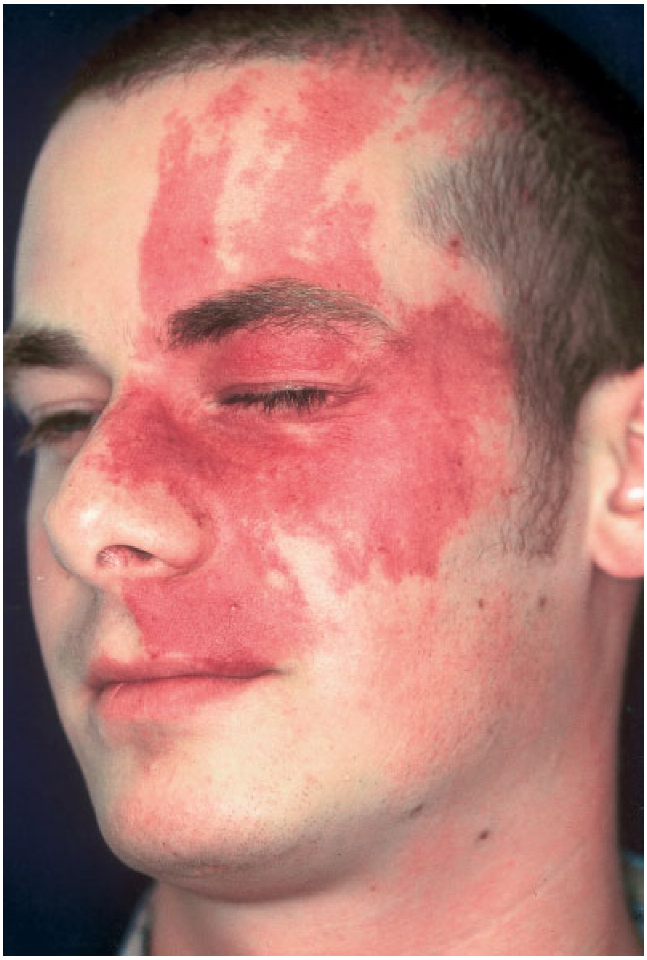
DISCUSSION

For many years, scientists in basic research and clinicians have addressed the topic of what constitutes the

TABLE 2. Localization, Color, and CS

			CS (nm/millisecond)		
Patient no.	Localization	Color	585/0.5	595/0.5	595/20
1	Leg	Purple	4	2	2
2	Face, neck	Purple	4	1	3
3	Back	Pink	2	2	2
4	Cheek	Red	3	2	1
5	Neck	Purple	2	1	2
6	Face	Red	2	1	2
7	Lip	Red	2	1	2
8	Neck	Red	1	1	4
9	Leg	Red	3	2	1
10	Face	Purple	4	3	2
11	Cheek	Red	4	3	2
12	Face, neck	Pink	2	1	1
13	Arm	Red	3	2	2
14	Forehead	Pink	1	1	3
15	Cheek	Pink	3	2	2
Mean CS			2.7	1.7	2.1

A



B

Fig. 2. **A**: PWS before treatment. **B**: Four weeks after the treatment. **Forehead**: 585 nm/0.5 milliseconds (CS = 2), **middle**: 595 nm/0.5 milliseconds (CS = 1), **temple**: 595 nm/20 milliseconds (CS = 2). [Figure can be viewed in color online via www.interscience.wiley.com.]

optimal treatment parameters for PWS [18–21]. The first commercially available pulsed-dye lasers emitted light at a wavelength of 577 nm, which corresponds to one of the absorption maximums of oxygenated hemoglobin. The other relevant absorption maximums of 415 and 542 nm are not as important because of the increased melanin absorption accompanied by concomitant minimized depth of penetration. In the late 80s, a switch was made from 577 nm to 585 nm after Tan et al. released a 1989 in vivo study on an albino pig skin, which demonstrated that the depth of penetration could be increased from 0.5 to 1.2 mm without affecting vascular selectivity [22]. Contrary to expectations, in this study, it was also shown that at a wavelength of 590 nm, there was no significant increase in depth of penetration; at the same time, however, at 590 nm and the same fluence, there was greater dermal tissue damage than at 585 nm.

TABLE 3. Color and CS

Color	CS (nm/millisecond)		
	585/0.5	595/0.5	595/20
Purple (n = 4)	3.5	1.7	2.5
Red (n = 7)	2.5	1.7	2.0
Pink (n = 4)	2.0	1.5	2.0

In terms of physics, the absorption coefficient of oxygenated hemoglobin is around four to five times higher at 585 nm as compared to 595 nm. The absorption coefficient of the epidermis, however, is more determined by the content of melanin than by a 10-nm difference in wavelength. The local volumetric production of heat in watts per unit volume equals the product of local absorption coefficient and local fluence rate, which is why the fluence must be increased when longer wavelengths are used with a pulsed-dye laser. This has been evaluated by different authors [13,15–17], although only Edström and Ros examined the clearance and side effects of 585 and 600 nm at constant fluences in clinical application. Since 600 nm is further away from the

TABLE 4. Purpura and CS

Parameter (nm/millisecond)	Purpura and CS							
	+++	CS	++	CS	+	CS	−	CS
585/0.5	9 (60%)	2.7	5 (33%)	1.8	—	—	1 (7%)	4
595/0.5	1 (7%)	1	4 (27%)	2.25	5 (33%)	1.4	5 (33%)	1.4
595/20	—	—	6 (40%)	2.5	7 (46%)	1.8	2 (14%)	2.0

+++, very strong; ++, strong; +, weak; −, not present.

absorption maximum of oxygenated hemoglobin than 595 nm is, we made a deliberate decision to compare 595 and 585 nm as well while maintaining the same pulse duration and fluence; our goal was to examine how PWS clearance was affected when the wavelength was shortened by only 10 nm.

As was the case with a setting of 600 nm, a wavelength of 595 nm with a pulse duration of 0.5 milliseconds and no increase of the fluence showed the poorest CS, although the rate of adverse effects was lowest here. Even when the fluence was increased to 13 J/cm^2 (and the pulse duration increased correspondingly), the same clearance still could not be achieved that was possible at 585 nm/0.5 milliseconds. It must be emphasized, however, that the spectrum of side effects worsened markedly as the fluence increased; here the side effects were comparable with those at a setting of 585 nm/0.5 milliseconds. For this reason, using a pulsed-dye laser at wavelengths >585 nm and longer pulse durations without concomitant epidermal cooling (cryogen spray or cold air) is not possible. Additional studies must be performed to determine to which extent the fluences can be increased (in conjunction with cooling) to ensure patient safety. A current study by Kelly et al. showed that pulses of 6–15 J/cm^2 at 7 or 10 mm in conjunction with cryogen-spray cooling can be used safely [23], but to what extent the use of higher fluences improves treatment efficacy could not be proved [23]. On the other hand, there was no evidence that either cryogen spray or cold air had a negative effect on clearance [24–28].

TABLE 5. Adverse Effects

Parameter (nm/millisecond)	+	+/−	−
Pain			
585/0.5	14 (93%)	—	1 (7%)
595/0.5	9 (60%)	4 (27%)	2 (13%)
595/20	14 (93%)	—	1 (7%)
Crusting			
585/0.5	5 (33%)	—	10 (67%)
595/0.5	—	—	15 (100%)
595/20	3 (20%)	—	12 (80%)
Hypopigmentation			
585/0.5	1 (7%)	—	14 (93%)
595/0.5	—	—	15 (100%)
595/20	—	—	15 (100%)
Hyperpigmentation			
585/0.5	—		15 (100%)
595/0.5	—		15 (100%)
595/20	—		15 (100%)
Scars	—	—	15 (100%)

+, clearly defined; +/−, weakly defined; −, not present.

From a clinical perspective, we see no advantage of 595 nm versus 585 nm in the initial treatment of PWS. Once again, we emphasize that the study only included patients with light skin types who were undergoing initial treatment of (PWS). After 585 nm has been used for multiple treatments and a clearance plateau is reached, it can be beneficial to try other wavelengths and/or pulse durations, presumably because different vessels may respond. Other authors have also been unable to prove the superiority of longer wavelengths in treating PWS [14,15, 17]. Unfortunately, it was not possible to compare the fluences (and thus the rate of adverse effects) due to the different spot sizes used in these studies.

Theoretical considerations state that the pulse duration has a significant effect on the clearance rate of PWS. Studies from Dierickx et al. indicate that the ideal pulse duration for PWS with an average vascular diameter of 30–150 μm is around 1–10 milliseconds [10]. Interestingly, Scherer et al. had the best clearance rate in 13 of 62 patients when they applied settings of 585 nm and a constant pulse duration of 1.5 milliseconds (compared with wavelengths of 590, 595, and 600 nm) [17]. A PWS that did not respond to standard treatment with the conventional pulsed-dye laser was significantly lightened by Bernstein et al. when they increased the pulse duration to 1.5 milliseconds (585 nm, 7 mm, 9 J/cm^2) [29].

Lou and Geronemus evaluated different pulse durations of a 595-nm pulsed-dye laser with cryogen-spray cooling in two patients [16]. The best clearance rate overall was found in the areas with the strongest postoperative purpura, which in turn correlated only with the extent of the fluence. Patient 2 (in the study of Lou and Geronemus) had epidermal atrophy at parameters as low as 1.5 milliseconds/13 J/cm^2 (7 mm) in spite of cooling. At a pulse duration of 20 milliseconds and 13–15 J/cm^2, the patients experienced only mild to moderate clearance.

With one exception (Patient no. 1), our study found a correlation between clearance and the extent of the purpura. It is interesting to note that when parameters of 595 nm/20 milliseconds are selected, purpura develops much more slowly (i.e., an average of 10 min) than at parameters of 585 nm/0.5 milliseconds (i.e., usually a few seconds after the pulse). Tanghetti et al. were also able to demonstrate this in a current study [30]. Assessing the therapeutic outcome and thus the maximum fluence is extremely difficult for the longer wavelength of 595 nm or pulse durations and would ultimately require a longer period of treatment.

In our study, results that were comparable to the conventional pulsed-dye laser were seen only in red and pink PWS at settings of 595 nm/20 milliseconds/13 J/cm^2. Purple PWS responded best to 585 nm/0.5 milliseconds. In contrast, Fiskerstrand et al. found in their clinical and histological study that red PWS with relatively superficial vessels, which are not too small in diameter, show the best results, and pink lesions with a very small diameter (15 ± 4.5 μm) show the worst [11]. Purple PWS, on the other hand, have very deep vessels and did not respond well to treatment with the dye laser.

The results of this study and clinical findings to date all indicate that the clearance of PWS is not decisively improved by longer wavelengths. This is also true for the range of adverse effects. An evaluation of pulse durations must be conducted in further studies. In our opinion, it would be interesting to increase the pulse duration in 585-nm pulsed-dye lasers, which has not been feasible yet for financial reasons.

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