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Role of 595nm PDL in Treating Port Wine Stains Resistant to 585nm PDL

MOHAMED MAHMOUD MAHMOUD ABD EL-AAL, M.D., A.B.L.S.

The Department of Plastic and Reconstructive Surgery, Faculty of Medicine, Ain Shams University.

ABSTRACT

Port wine stain (PWS) is a congenital progressive capillary vascular malformation under normal epidermis. The conventional pulsed dye laser (PDL), operating at a wavelength of 585nm and a pulse duration of 0.5ms, usually does not achieve complete clearance in the majority of hypertrophied port-wine PWS. In this study, we investigate the efficacy of 595nm PDL equipped with cryogen spray cooling (CSC) in the treatment of fourteen adult patients with hypertrophied facial PWSs that have become resistant to 585nm PDL treatment.

Patients were divided into two groups (seven patients each), according to the treatment parameters. All patients were treated by the same fluence (12 J/cm^2) but pulse width was 10 msec and 3 msec in group I and II respectively. Three to five sessions were done in each group every 8-12 weeks and all patients were followed for a minimum of 6 months after their last session.

Patients in group I showed insignificantly better lightening response as 6 patients (85.7%) had more than 50% clearance compared to 5 patients (71.4%) in group II had the same results after a mean of 3.66 and 4.2 treatment sessions' respectively. Therefore, we conclude that 595nm PDL can improve resistant PWS to conventional 585nm PDL especially when using higher fluencies with longer exposure time to target larger and deep vessels.

INTRODUCTION

Port wine stain (PWS) is a congenital progressive capillary vascular malformation that consists of abnormal plexus of dilated blood vessels in the upper dermis, under normal epidermis [1]. In childhood, PWSs are faint pink macules with no tendency to spontaneous resolution. In contrast they tend to get darker (red-purple) and often nodular due to progressive ectasia. The main etiologic factor is a deficit in the numbers of autonomic perivascular nerves resulting in failure to regulate blood flow [2].

Since two-thirds of these malformations occur in the face, PWSs are a clinically significant problem. PWSs should not be considered only as a cosmetic problem but a disease with potentially devastating psychological and physical complications [3].

In the past, different procedures were tried to treat PWSs such as skin grafting, ionizing radiation, dermabrasion, cryosurgery, tattooing, and electrotherapy, but none of these modalities provided cosmetically acceptable results [4]. The development of lasers open a new scope for the treatment of PWS based on selective photocoagulation of the ectatic vasculature. The pulsed-dye laser set to a wavelength of 585nm and pulse duration of 0.5 milliseconds has been a standard treatment of PWS since as early as 1980s. PWS response depends upon various factors (age, localization, size, color) and cannot generally be predicted [5,6,7].

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 the literature in approximately 14-40% of all cases [8,9,10]. Some referred these limitations and other side effects after 585nm pulsed dye laser (blistering, dyspigmentation, or scarring) due to non-specific absorption by melanin that induces epidermal heating. Despite the recent implementation of active skin cooling technology, melanin absorption limits the radiant exposure that can be safely applied in laser treatment, thereby adversely impairing the efficacy of PWS therapy in many patients [11,12].

The development of longer wavelength (595nm) and longer pulse width (up to 40msec) lasers should theoretically targeting larger caliber and more deeply situated vessels, results in more complete clearance of PWS. The associated dynamic cooling device enables the delivery of higher fluencies and provides protection of the epidermis and the superficial dermis from thermal damage thus reduces the treatment associated discomfort and pigmentary complications [13,14,15].

The aim of this prospective study is to investigate the effect of long pulsed dye laser (595nm) with high fluencies on previously treated PWS which no longer responded to conventional PDL (585nm, 0.5msec), whether further clearance could be achieved.

PATIENTS AND METHODS

Fourteen adult patients with facial PWSs were included in this study. All were complaining of hypertrophic (nodular), purple PWSs. All patients were previously received a minimum five treatment sessions with conventional PDL (585nm, 0.5msec), where no further clearance could be achieved after at least six month from the last session. Children were excluded with adult patients who had developed permanent hypo-or hyperpigmentation. The V-Beam Candela pulsed dye laser that operates at a wavelength of 595nm and provides discrete macro pulse duration up to 40ms was used in this study. Laser was delivered through an optical fiber and lens, which focused the beam onto a 7mm handpiece with 60% overlap. A Cryogen spray cooling (CSC) device is incorporated into the handpiece of this laser system. The CSC was set to administer a 40ms cryogen with 20ms delay before laser firing. No local or topical analgesia was used. After each session, topical antibiotic ointment was applied and patients were instructed to avoid direct sun exposures for at least 3 months.

Patients were divided into two groups (7 per each group), according to the treatment parameters. The first group was treated by 12 J/cm^2 and 10msec. The second group was treated by 12 J/cm^2 and 3msec. The laser treatment was repeated every 8-12 weeks with the same parameters. Number of treatments ranged from 3 to 5. Treatment was stopped if there is no further clinical improvement and all patients were followed for a minimum of 6 months after their last treatments.

Each patient was photographed by standard digital camera (Fuji S5000-FinePix, 10x optical zoom) before treatment starts, before the following session, and at six month after the last treatment. Clinical response was assessed by three neutral observers comparing the baseline photographs with those taken after laser treatments in percentage of lightening; Poor; 0-25%, Fair; 26-50%, Good; 51-75%, and Excellent; 76-100% (Table 1). The mean of three measurements was used for each analysis. Differences between the mean lightening response scores for both treatments groups were analyzed using a chi-squared test. Safety was also evaluated and analyzed using a chi-squared test between groups by looking for any adverse effects.

Table (1): Lightening response scoring following laser treatments.

Lightening score	% of lightening
1	Poor (>25%)
2	Fair (26-50%)
3	Good (51-75%)
4	Excellent (76-100%)

RESULTS

Ten women and four men with facial PWS, age ranges from 18-35years (mean of 23.92±5.38) were treated in this study. Excellent results with more than 75% clearance were achieved in 4 patients (57.1%) in the 1st group and in 3 patients (43%) in the 2nd group after a mean of 3.7 and 4.1 session respectively (Figs. 1,2). Two patients in each group (28.6%) showed good results, while one patient (14.3%) in first group and two in the second experienced poor to fair result (Tables 2,3).

The mean lightening response scores and standard deviations were 3.43±0.79 for group I and 3.0±1.15 for group II after a mean of 3.71±0.76 and 4.14±0.69 treatment sessions respectively, indicating an enhanced clinical lightening response in group I (Table 4). Although lightening response was more in group I with less number of sessions, this difference was statistically of no significance between the two groups based on chi-squared test ($p<0.05$).

Patients in group I experienced superficial ulceration and crustation which heal within 7-14 days, while healing occurred within the first week in group II. Side effects were common in group I (57.1%), three patients developed transient hyperpigmentation, therefore interval between sessions were extended up to three months and patients were instructed to use sun protective and bleaching creams. One patient in this group (skin type V) developed atrophic scar after healing of ulcerated skin over left malar area. In group II, only one patient developed transient hyperpigmentation with no signs of scarring. There was no statistical difference in overall complications in both groups (Table 5).

Fig. (1): 35 year male patient after 4 sessions with more than 75% clearance in group I.

Fig. (2): 22 year female patient after 5 sessions with more than 75% clearance in group II.

Table (2): Group I (12J/cm^2, 10msec.).

Gender/ age	Skin type	No. sessions	Clearance	Side effects
M/35	III	4	Excellent	Hyperpigmentation
F/18	IV	3	Excellent	Hyperpigmentation
F/19	III	3	Excellent	–
F/21	III	3	Excellent	–
F/25	V	5	Good	Atrophic scar
F/30	II	4	Good	–
M/25	IV	4	Fair	Hyperpigmentation

Table (3): Group II (12J/cm^2, 3msec.).

Gender/ age	Skin type	No. sessions	Clearance	Side effects
M/18	IV	4	Excellent	–
F/20	IV	4	Excellent	–
F/22	II	5	Excellent	–
F/28	III	3	Good	–
F/25	IV	5	Good	–
M/19	III	4	Fair	–
M/30	IV	4	Poor	Hyperpigmentation

Table (4): Statistical differences in lightening response scoring between the two groups.

	G (I)		G (II)	
	Sessions	Lightening score	Sessions	Lightening score
Poor	–	–	4	1
Fair	4	2	4	2
Good	9	6	8	6
Excellent	13	16	13	12
Mean±SD	3.71±0.76	3.43±0.79	4.14±0.69	3.0±1.15

$p<0.05$.

Table (5): Statistical differences in complication scoring between the two groups.

Side effects	Group I (n=7)		Group II (n=7)		*p* value	Sig.
	No.	%	No.	%		
None	3	42.9	6	85.7	>0.05	NS
Atrophic scar	1	14.3	0	0		
Hyperpigmentation	3	42.9	1	14.3		

DISCUSSION

PWS is a congenital pink vascular skin malformation which may progress into darker (purple) hypertrophied nodular lesion in adulthood. The clinical response in PWS laser therapy based on, selective thermal destruction of ectatic dermal dilated vessels in the upper dermis. Pulsed green or yellow lasers were introduced in the treatment of PWS as a selective tool that absorbed by oxyhemoglobin inducing irreversible photothermal damage to vessel walls. Many lasers were used in the treatment of PWS but PDL has been the treatment of choice. The first available commercial PDL emitted light at a wavelength of 577nm but shift was made to 585nm PDL after a study demonstrated increase depth of penetration from 0.5 to 1.2mm without affecting vascular selectivity **[16]**.

Patient age, skin coloration, and PWS characteristics; anatomic location, size, surface and color are prognostic indicators of PDL as regard number of treatment sessions and final clearance. Many treatments are needed with an interval of 2 to 3 months to achieve good results, however, clearance rates vary widely after 585 PDL and many lesions are not completely cleared. In theory, it is difficult to treat PWS using a fixed, short pulse width. In the other hand, the laser pulse should be long enough to heat the vessel wall, but short enough to prevent excessive heating of perivascular tissues. Ideally, pulse duration should be equal or less than the thermal relaxation time of the targeted vessels (the required time for the absorbed energy to be conducted into the vessel wall). A wide range of vessel sizes exist in PWS within different vascular layers ranges from 10µm to 100µm **[17]**.

Clinical results with conventional 0.5-ms 585-nm PDL-treated hypertrophied nodular PWS composed of large vessels are frequently insufficient. PDL-resistant PWS have been reported using also the 1.5-ms 585-nm PDL **[14,18]** and intense pulsed light source **[19]** (wavelength spectrum of 550-1200nm). Some vessels within PWS may be too large in diameter or may carry blood too quickly, and hence, low energy and short pulse cannot damage coagulated large vessels irreversibly that subsequently regenerate. Also, 585-nm wavelength does not penetrate deep enough to target deeper dermal vessels in PWS with multiple vascular layers **[20]**. There is also a suggestion that the formation of a fibrous shield in the upper papillary dermis (generated by destroyed superficial vessels from previous PDL treatment) might progressively obstruct laser light in subsequent treatments from penetrating into the deeper dermal vessels **[21]**.

Improved treatment is expected by utilizing higher fluencies **[22,23]**, longer pulse durations **[14]**, and longer wavelength **[24,25]**. Increasing fluencies will increase the laser induced temperature within the targeted blood vessels, resulting in improving clearance, and longer pulse durations are more effective for damaging larger blood vessels. Longer wavelengths in the visible spectrum are likely to penetrate deep and produce deeper vascular coagulation. For example, increasing wavelength from 585nm to 595nm will increase the light penetration depth in blood from approximately 50µm to 260µm **[26]**. But since hemoglobin absorption coefficient decreases with longer wavelengths, higher fluencies are necessary with these wavelengths **[27]**. Higher fluencies will also result in increased temperature within the epidermis, and subsequently increase the risk of non-specific thermal damage to the epidermis. Therefore, cryogens spray cooling (CSC) in conjunction with laser irradiation offers a method to protect the overlying epidermis **[28]**. In our study, a short cryogen spurt 40sec was sprayed onto the skin surface immediately prior to the onset of laser pulse (20msec delay) which cooling the epidermis while the targeted blood vessels are not affected by the cold wave.

Patients can tolerate higher fluencies when using 595 nm (7-15 J/cm^2), compared to 585nm (7-10 J/cm^2), when the pulse duration (1.5ms), spotsize (7mm), and skin cooling remain constant. In studies comparing the highest tolerated dose of each wavelength, the 595-nm PDL provides superior PWS lightening when compared to 585nm. [14,19].

Purpura is one of the end points when treating PWS. In 2006, Asahina and coworkers [29] reported that there was a good correlation between clearance of PWS and the mean intensity of immediate purpura observed after each of the multiple treatment sessions when using a PDL. The end point of 595nm PDL is also purpura. The lowest fluencies that caused purpura and were seen in more than 50% of patients were 10 J/cm^2 with pulse duration of 1.5ms, 12 J/cm^2 with pulse duration of 3ms, 13 J/cm^2 with pulse duration of 6 and 10ms. In our study it was also noted the development of immediate purpura in both groups with higher fluencies and longer pulsewidth and all patients showed high tolerability as no local anesthesia was used.

Rohrer and colleagues [30] used a 595 PDL to demonstrate that pulse stacking at pulse duration of 10ms can increase vessel clearance, when compared to single pulses of the same fluence. They also reported that pulse stacking was more likely to cause edema, but otherwise do not significantly increase the risk of dyspigmentation and scarring. We have applied this pulse-stacking technique to enhance the efficacy of our treatments. In our study, minor transient side effects were observed especially in first group. However, there were no statistical differences between the two groups as regard the incidence of complications.

In our study, the 595 PDL operating at higher fluencies (12 J/cm^2) at variable longer pulse durations (3 or 6ms) and using the pulse-stacking technique appears to treat larger diameter and deeper dermal capillaries that are not treated by the 585-nm 0.5-ms PDL.

It is also possible that extending the treatment course with the 595-nm PDL may further improve apparently treatment-resistant PWS. Kauvar and Geronemus [31] studied 69 PWS patients who had failed to achieve more than 75% lightening with nine treatment sessions and reported that further lightening could be achieved with continued PDL treatments, up to 25 sessions. Verkruysse and coworkers [32] demonstrated that multiple, consecutive laser pulses target deeper and more optically shielded blood vessels. This treatment strategy may help treat PDL-resistant PWS.

Vessels less than 30mm are resistant to treatment from both the 585-nm PDL and the 595-nm PDL as small vessels do not contain enough red blood cells and are therefore poor targets for these lasers. In an attempt to enhance efficacy, the technique of multipassing, pulse stacking, or pressure therapy may play a role in the treatment of small vessels in PWS [27,33,34]. The long-pulse 1064-nm Nd:YAG laser 15 has been used effectively to treat deeper, larger diameter vessels, such as leg veins, and may have a role in treating PDL-resistant PWS [35].

In conclusion, selection of optimum laser parameters is crucial for successful laser therapy of PWS based on vessels diameter, depth, and skin color. In general, smaller blood vessels should be treated using shorter wavelength such as 585-nm, while larger venules better to be treated by longer wavelengths and higher fluencies such as 595-nm with optimizing the CSC parameters for epidermal protection. PWS treatment protocol has become more complicated recently secondary to laser manufacturers introducing devices that allow the operator to vary several treatment parameters such as wavelength, pulse duration, energy, and skin cooling. Further studies are warranted to find the optimal treatment parameters for PWSs.

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