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Treatment of port wine stain by flash-lamp pulse-dye laser 595 nm

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Abstract
Introduction: Port wine stain (PWS) is one of the commonly encountered congenital cutaneous vascular lesions, with an equal sex distribution. Pulsed-dye lasers (PDL) have revolutionized the treatment of both congenital and acquired cutaneous vascular lesions. The pulsed dye laser owing to its superior efficacy and safety profile have become the appropriate choice for the management of port-wine stains.
Aim: To evaluate the efficacy and side effects of pulse dye laser in the treatment of port wine stain.
Patients and Methods: This is a prospective interventional therapeutic study, which was conducted at the Center of Dermatology and Venereology, Medical City in Baghdad/Iraq, from February 2020 to January 2022. Patients with port wine stain who attended the dermatology outpatient clinic were included in this study, their demography had been assessed, facial port wine area and severity index (FSASI) was done for their PWS and photos for documenting the results were taken. Pulse dye laser session was done for 30 patients for 3 to 10 sessions on monthly basis. Therapeutic outcomes were assessed by standardized digital photography.
Results: A total of 26 patients completed the study, 17 (65, 4%) females and 9 (34, 6%) males. Age ranged from 3 to 62 years. Eight patients reported excellent improvement (76-99%), thirteen patients' significant improvement (51-75%), five patients with moderate improvement (26-50%) in the appearance of the PWSs.
Conclusions: Pulse dye laser is a good modality of treatment for PWS being a safe and effective option in Iraqi patients.

Keywords: Treatment, port, wine, stain, flash-lamp, pulse-dye, laser

Introduction

Vascular anomalies, conditions characterized by aberrant endothelial behavior, are broadly classified into vascular tumors and vascular malformations, which are characterized by proliferative and quiescent endothelium, respectively. These anomalies, affecting individuals across all age groups, often require comprehensive diagnostic expertise and multidisciplinary management due to their complexity [1]. The field of vascular anomalies has seen considerable progress with the establishment of a universally accepted terminology, eschewing the imprecise jargon previously used. The advent of Mulliken and Glowacki's classification system in 1982, which was subsequently integrated into the International Society for Study of Vascular Anomalies (ISSVA) classification system, has helped clinicians and researchers bring precision to the diagnosis, treatment, and research of these conditions [2, 3]. The ISSVA classification system, now widely accepted, forms the basis for diagnosing and treating vascular anomalies. These include vascular tumors such as hemangiomas and vascular malformations, which are further classified based on their vascular components into simple and combined malformations. These anomalies can be distinguished based on their biological behavior, clinical appearance, and radiological and pathological features [3]. Capillary malformations or port wine stains (PWS) are congenital vascular lesions affecting the skin. They often result in significant psychological distress, particularly when located on the face. Early intervention, ideally before the commencement of formal education, can help prevent psychological impairment and potential complications [4]. The advent of the flash lamp pulsed dye laser, specifically designed for cutaneous vascular lesions, has revolutionized the treatment of PWS, as it minimizes the risk of scarring

or depigmentation [5]. Vascular malformations, a less common subtype of vascular anomalies, are characterized by developmental errors in vascular formation. These malformations, which affect 0.3% to 0.5% of the population, are distinct from hemangiomas, and are not gender-biased. While present at birth, unlike hemangiomas, they do not undergo rapid growth and subsequent involution. Instead, they tend to grow in proportion to the child, often becoming more prominent during puberty. Moreover, certain placenta-associated vascular antigens, including GLUT1, a human glucose transport protein, serve as sensitive and specific markers for hemangiomas and are absent in vascular malformations [6]. Vascular malformations are further categorized based on their flow characteristics and primary vascular component, distinguishing between slow-flow and fast-flow lesions [6].

Aim of the study

To evaluate the effectiveness and side effects of pulse dye laser in the treatment of port wine stain.

Method

This study was a prospective, interventional therapeutic study conducted at the Center of Dermatology / Venereology in Baghdad, Iraq, from February 2020 to January 2022. Thirty patients presenting with port wine stain (PWS) were initially recruited for laser treatment. However, only 26 patients completed the study. Ethical considerations were duly maintained by obtaining informed consent from the participants or their parents, and the study was ethically approved by the scientific council of Dermatology and Venereology/Arab Board for Medical Specializations. Patients with facial and neck PWS were included in the study, while pregnant women, patients with clinically diagnosed hemangiomas, children below 3 years, and individuals with doubtful diagnosis, among others, were excluded. Patient history and thorough examinations were undertaken, and photos of the PWS were taken using a mobile phone camera. Each patient underwent a detailed consultation, which included counseling regarding the outcomes and recovery period of the procedure. The treatment involved applying a topical anesthetic, EMLA, followed by laser treatment using a Vbeam Perfecta laser system. Protective measures such as goggles were used to ensure patient safety. Patients were also given post-treatment care instructions, which included the application of topical antibiotics and sunblock. Each patient was treated with a single laser session, and the treatment parameters were customized in every session. All patients were photographed before and after each treatment session, and the outcomes were evaluated using the Facial Port-wine Stain Area and Severity Index (FSASI) and a Visual Analog Scale (VAS). Three different doctors were engaged to independently evaluate the improvement in PWS blanching. The collected data were statistically analyzed using the Statistical Package for the Social Sciences (SPSS) version 23. Descriptive analyses were conducted focusing on frequencies, percentages, means, and standard deviation. Associations between qualitative and quantitative variables were determined using Fisher Exact Test and correlation tests, respectively, considering a P-value $\leq$ 0.05 as statistically significant.

Results

All participants had port wine stain on face and neck, in a period of 23 months; from early February 2020 to January 2022, a total of 26 individuals were enrolled in this study, among them 17(65.4) were females and 9 (34.6) were males, female: male ratio was 1.8: 1. The age varied from 3 years to 62 years with mean value 24.26±2.93 (14.97), the median was 59 (3-62). As shown below in table (1).

Table 1: Demographic dataset of the patients.

Variable		No. (%)
Age groups	1-14	4 (15.4)
	15-40	19 (73.1)
Age (years)	41 and more	3 (11.5)
Mean ± SD (SE) Range (Minimum-Maximum)	24.26±2.93 (14.97) 59 (3-62)	
Gender	Male	9 (34.6)
	Female	17 (65.4)
Consanguinity	Negative	16 (61.5)
	Positive	10 (38.5)

The diagnosis was clinical in all of the cases. In this study 1 (3.8%) patients had family history of the same condition. Skin type in 70% of cases were Fitzpatrick skin type 3 and the rest was skin type 4. Some of the lesions; 1 (3.8%) were treated before by one session laser in a private clinic, and 25 lesions (96.1%) were untreated at time of presentation. There was one patient (3.8%) had two port wine stain at the same time port wine stain. Of note: there was one patient who had cataract (and Glaucoma unilateral to the affected site), diagnosis of SWS was ruled out by imaging and consultations. Three patients had PWS covering half face; their lesions spread over wide areas of the neck with ill-defined margins so the number of lesions was considered as one for each of them for statistical analysis. All lesion was asymptomatic, there was no bleeding or pain. All lesions presented since birth and the diagnosis was clinical. Treatment of PWS with PDL led to darkening of vascular structures (immediately) the clinical target response (purpura) followed by the appearance of white area normal skin representing disappearance of vascularity (after two weeks). 26 patients (17 females and 9 males) were included in this study, including the 6 months' follow-up period. According to dermatologists' assessment shown in table (2) and figure (1), the results were 5 patients had obtained 26-50% improvement, 13 patients with 51-75%. Reported good improvement and 7 patients had reached 76-99% reported excellent improvement. Age group from 3 to 62 years we divided them into three categories (as shown in figure 1): 4 patients from age group (1 to14 years), 19 patients (15 to 40 years) and 3 patients from (41 and more). Ten out of 26 patient showed positive consanguinity (their parents are of relative marriage) while the rest (16 patient) reported

negative consanguinity. Sex of the participants: male 9 (34.6%) and female 17 (65, 4%). On the other hand, the patients' final assessment of improvement according to consanguinity was also remarkable and showed a 7 patients out of 16 of those with negative consanguinity showed excellent improvement in contrast no one showed excellent result in those of positive consanguinity, with a P value of <0,05 being significant.

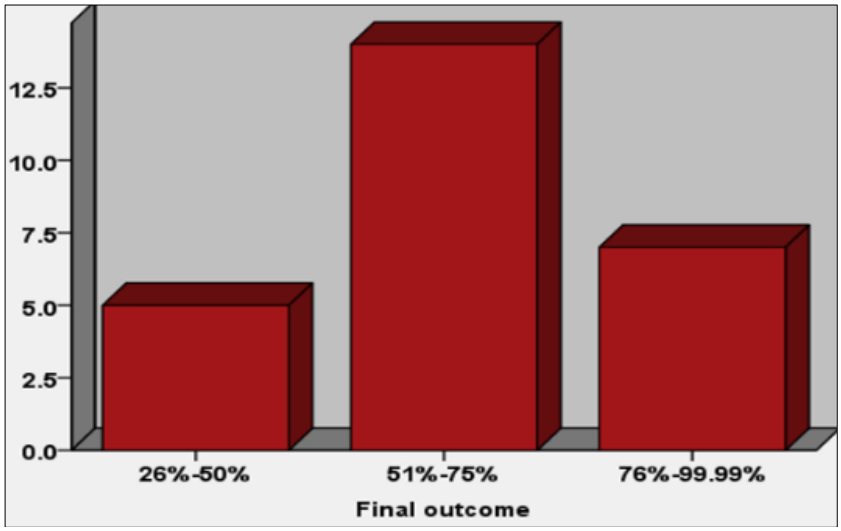

Fig 1: Final outcome & improvement in PWS

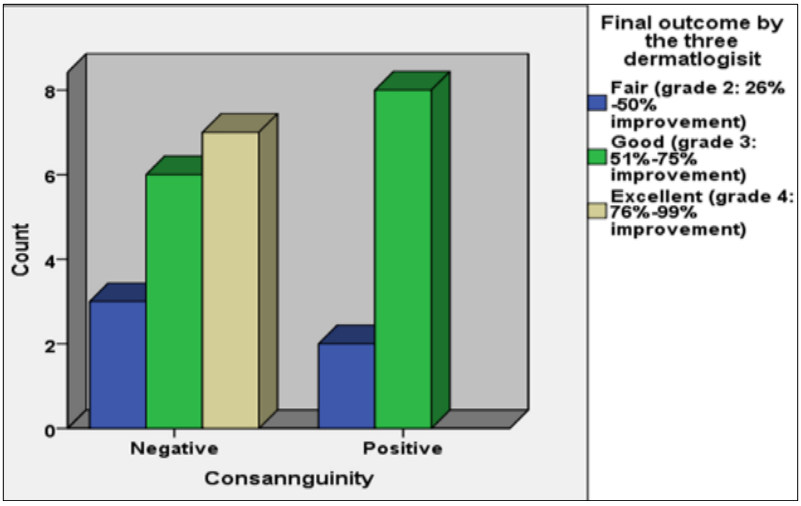

Fig 2: final outcome according to consanguinity

Table 2: Final outcome by the socio demographic characteristics of the study

		Final outcome by the three dermatologists			
		Fair	**Good**	**Excellent**	**Total**
Sex	Male	3 (33.3%)	4 (44.4%)	2 (22.2%)	9 (100%)
	Female	2 (11.8%)	10 (58.8%)	5 (29.4%)	17(100%)
	Total	5 (19.2%)	14 (53.8%)	7 (26.9%)	26(100%)
Age groups (years)	1-14	0 (0%)	2 (50.0%)	2 (50.0%)	4 (100%)
	15-40	4 (21.1%)	10 (52.6%)	5 (26.3%)	19(100%)
	41-99	1 (33.3%)	2 (66.7%)	0 (0%)	3(100%)
	Total	5 (19.2%)	14 (53.8%)	7 (26.9%)	26(100%)
Consanguinity	Negative	3 (18.8%)	6 (37.5%)	7 (43.8%)	16(100%)
	Positive	2 (20.0%)	8 (80.0%)	0 (0%)	10(100%)
	Total	5 (19.2%)	14 (53.8%)	7 (26.9%)	26(100%)

Table 3: Final outcome by the three dermatologists

		Fair	**Good**	**Excellent**	**Total**	**p-value***
Consanguinity	Negative	3	6	7	16	<0.05
	Positive	2	8	0	10	
	Total	5	14	7	26	

*Four cells (66.7%) have expected count less than 5. The minimum expected count is 1.92, Significant association using Fisher exact test at 0.05 level.

Significant improvement occurred in the age group between 15 -40 years more than the other age categories (1-14 years and 41-99 years) but still age is not correlated to treatment response of port wine stain and the P value was insignificant as shown in figure (3) & table (4).

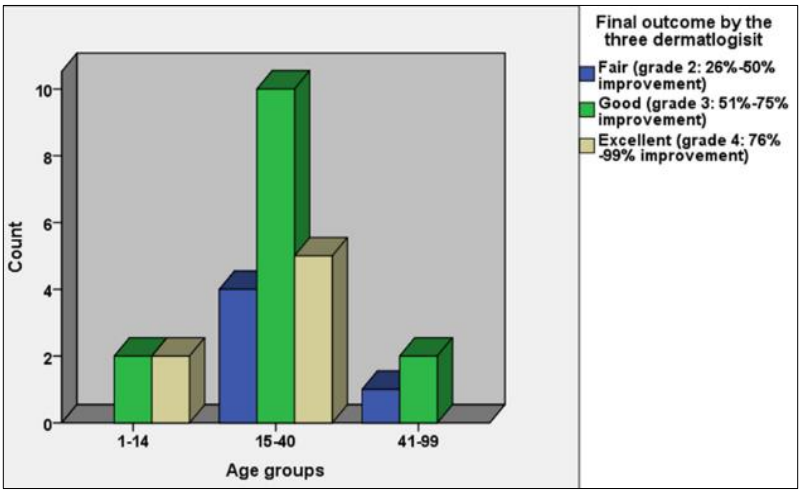

Fig 3: Final outcome according to age group

Table 4: Final outcome by the three dermatologists (According to age group)

Final outcome by the three dermatologists						
		Fair	**Good**	**Excellent**	**Total**	**p-value***
Age groups (years)	1-14	0	2	2	4	>0.05
	15-40	4	10	5	19	
	41-99	1	2	0	3	
	Total	5	14	7	26	

* Seven cells (77.8%) have expected count less than 5. The minimum expected count is. 58, Significant association using Fisher exact test at 0.05 level.

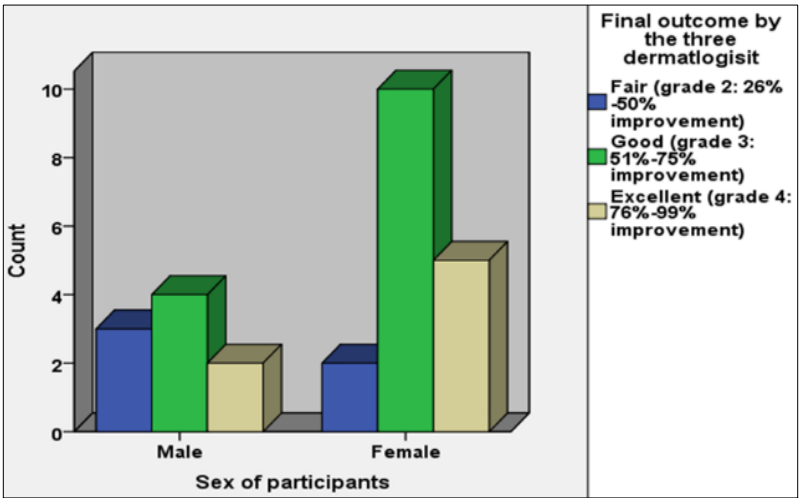

Fig 4: Final outcome according to sex of participants

The improvement scale was not significant for the gender, female with excellent response were five, with good response ten and fair group was only two. While the male three with fair response, five with good response and two with excellent response. As a result there is no significant correlation between sex of participant, and the P value was >0, 05. Thus outcome were almost comparable to the dermatologists' assessment as shown in figure (5) & table (6).

Table 5: Final outcome

Final outcome						
		Fair	**Good**	**Excellent**	**Total**	**p-value***
Sex	Male	3	4	2	9	>0.05
	Female	2	10	5	17	
	Total	5	14	7	26	

* Five cells (83.3%) have expected count less than 5. The minimum expected count is 1.73., significant association using Fisher exact test at 0.05 level.

Table 6: number of laser session for each patients and their improvement.

Patient numbers	Number of sessions	Clearance percentage	Patient numbers	Number of sessions	Clearance percentage
1	9	50%	14	10	80%
2	10	70%	15	10	40%
3	10	65%	16	8	65%
4	10	55%	17	8	78%
5	10	75%	18	9	50%
6	10	55%	19	3	95%
7	10	70%	20	6	65%
8	10	65%	21	8	40%
9	8	45%	22	5	75%
10	10	70%	23	7	70%
11	10	89%	24	6	85%
12	5	75%	25	6	90%
13	10	75%	26	4	99%

Safety

In general, unremarkable side effects were noticed. Participants experienced swelling and pigmentation of purpura. Beside, post inflammatory hyperpigmentation was seen in 6 out of 26 participants due to their dark skin type, later managed at the end of treatment course with bleaching agent. All patients suffered from some degrees of pain from pulse dye laser the majority with mild degree of pain 60%, while 30% expressed moderate degree of pain and no one with severe pain. While scarring, hypopigmentation, or infection had not been reported.

a) Before b) After

Fig 1: a) Before laser treatment, b) After laser treatment (10 session)

a) Before b) After

Fig 2: a) Before laser treatment, b) After 4 session of laser treatment

Discussion

Port-wine stains (PWS) exhibit varying responses to pulsed dye laser (PDL) therapy across different body sites. Central facial areas often respond less favorably to PDL than other sites such as the upper face, around the eye, lateral cheek, chin, and neck. A possible explanation involves the varying types and depths of blood vessels present in different PWS sites. Studies using the Visual Analogue Scale and the Facial Port-Wine Stain Area and Severity Index (FSASI) scoring system suggest that PWS on the lateral face respond

better to therapy than those on the central face [7, 8]. Yu W *et al*.'s histological analysis showed that PWS features differ according to site. Central facial PWS, for example, typically have larger and deeper capillaries than lateral facial PWS. PDL's effectiveness depends on these vascular characteristics and the degree of light scattering, which also varies by location and increases with age [7]. The treatment outcomes of PWS also differ based on other factors. For example, the neck and periorbital regions are more likely to scar or blister following PDL treatment. The color and texture of PWS also affect outcomes: lighter, net-like PWS respond better than darker, geometric ones. Similarly, flat PWS yield better results than nodular, overgrown ones [9]. Treatment responses also vary with the anatomical distribution of PWS. For instance, PWS in the V1 distribution (opthalmic division of the trigeminal nerve) generally respond well to PDL therapy, possibly due to the peculiar vascularization pattern of this area [10]. Age is another factor affecting PDL responses. Although van der Horst *et al*. suggested age was not a significant determinant of therapy timing [11], Wenhao Shi *et al*. argued that younger patients generally achieve better results due to lower dermal thickness and less melanin and collagen in the skin [12]. Recalcitrant PWS (those resistant to treatment) can be a challenge, but larger laser spot sizes (>12 mm) might improve outcomes in these cases [13]. Furthermore, acquired PWS generally responds better to PDL therapy than congenital PWS [14]. Treatment intervals also affect outcomes. Shorter intervals can hasten results, but may also increase the risk of scarring [15]. In this study, a 4-week interval was chosen to allow post-laser purpura to heal and reduce side effects [16]. After a certain number of treatments (6 to 10), a plateau effect is often observed, where further treatments yield no additional improvement [17]. This could be due to the inability of the laser to reach deeper vessels, the development of a fibrous shield in the upper papillary dermis, or the presence of large, high-flow vessels. Finally, some PWS are recalcitrant to laser therapy, necessitating specific laser settings based on their morphological features. Factors such as PWS thickness, anatomical site, area size, and individual age may contribute to this resistance [18].

Conclusion

Although good result and convincing clearance, but there is no promises of optimal outcome. The number of session should be between 3 to 10 sessions because there was no further improvement, so not to exceed the 10th session. We start by the lowest effective fluency that gave us the clinical end point (the purpura) and then increase subsequently thereafter in the upcoming session.

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