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Evaluation of the Success of Pulsed Dye Laser 595nm in the Treatment of Rosacea

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Abstract

Rosacea is a common, chronic inflammatory skin condition characterized by erythema, flushing episodes, and inflammatory lesions. Light-based treatments available with great fame in the management of rosacea, notably pulsed dye lasers (PDL), have revolutionised the management of rosacea. This is a prospective therapeutic intervention study done at the Centre of Dermatology and Venereology, Medical City, Baghdad, Iraq. The patients included fifty patients with Erythematotelangiectatic Rosacea (29) and Papulopustular Rosacea (21). Sessions of pulsed dye laser were administered in between 2 and 6 sessions monthly, and the time of follow-up was three months after the last session. Fifty participants completed the research. The majority of subjects were females (84%). In the group, 58% had erythematotelangiectatic rosacea and 42% papulopustular rosacea. Paired samples t-test over 20 months of research showed a significantly better response of each subtype of the disease (P=0.000). Also, the difference in response based on the subtype of rosacea was meaningful in favor of the papulopustular group (P=0.000). Pulsed dye laser therapy is effective and safe in the management of both erythematotelangiectatic and papulopustular subtypes of rosacea, with significant results, particularly noted in papulopustular rosacea, but without significant side effects.

Keywords: Pulsed, Dye Laser, Rosacea.

Introduction

Rosacea is the most common chronic inflammatory skin disease, exhibiting persistent erythema of the central convex face in a distribution over an area with chronicity for at least three months. The symptoms are primarily facial flushing, and clinical signs include redness, visible blood vessels, an inflammatory eruption of papules and pustules, and coarseness of the skin. Areas principally involved include the cheeks, nose, chin, forehead, and eyes, with periods of exacerbation and remission [1].

Generally affecting fair-skinned or even light-skinned individuals who are vulnerable to sunlight, rosacea is generally common in individuals of middle age, aged between 30 and 50. It is very pertinent to note that up to one-quarter of patients with rosacea have a family history of the disease [2]. Far-reaching worldwide epidemiological studies hint that the prevalence of the disease is around 5.5% of the world's population [3], with the incidence being at a maximum of 18%, especially in populations of Celtic origin. This accounts for about

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1% of all the skin conditions diagnosed by dermatologists [4]. Most forms of rosacea afflict both genders almost in equal proportions, except for the phymatous type of rosacea, which tends to afflict males more [5].

New classification

It is emphasized that the diagnosis of this disease can only be confirmed if there is one characteristic criterion or, in the absence of it, two or more of the basic phenotypic signs. With this approach, the broad clinical variability of rosacea is presented in Table 1.

Table 1: Updated Classification Based on Phenotypes of Rosacea [6].

Diagnostic Features	Major Features	Minor or Secondary Features
• Fixed centrofacial erythema in a characteristic pattern that may periodically intensify • Phymatous changes	• Flushing • Papules and pustules • Telangiectasia • Ocular manifestations: • Lid margin telangiectasia • Interpalpebral conjunctival injection • Spade-shaped infiltrates in the cornea • Scleritis and sclerokeratitis	• Burning sensation • Stinging sensation • Edema • Dryness • Ocular manifestations: • "Honey crust" and collarette accumulation at the base of the lashes • Irregularity of the lid margin • Evaporative tear dysfunction (rapid tear breakup time)

TREATMENT:

Patient education should be carried out in the first clinical consultation regarding the chronic nature of rosacea with an even course but with relapse, hence calling for continuous therapeutic measures, including maintenance treatment during periods of remission.

Table 2: A rosacea treatment program based on different characteristics of the skin, as per the recommendations of the Rosacea Consensus Panel consensus statements [7].

<table>
<tr><td rowspan="2">Transient erythema[a]</td><td rowspan="2">Persistent erythema[b]</td><td colspan="3">Inflammatory papules/pustules</td><td rowspan="2">Telangiectasia</td><td colspan="2">Phyma</td></tr>
<tr><td>Mild</td><td>Moderate</td><td>Severe inflamed</td><td>inflamed</td><td>Clinically noninflamed</td></tr>
<tr><td>a-adrenergics (topical)</td><td>Brimonidine (topical)</td><td>Azelaic acid (topical)</td><td>Azelaic acid (topical)</td><td>Ivermectin (topical)</td><td>Electrodessicat ion</td><td>Doxycycline (oral)[c]</td><td rowspan="4">Physical modalities</td></tr>
<tr><td rowspan="3">Beta blockers (oral)</td><td>IPL</td><td>Ivermectin (topical)</td><td>Ivermectin (topical)</td><td>Doxycycline(o ral)[c]</td><td>IPL</td><td rowspan="3">Isotretinoin (oral)</td></tr>
<tr><td rowspan="2">PDL</td><td>Metronidazole (topical)</td><td>Metronidazole (topical)</td><td rowspan="2">Isotretinoin (oral)</td><td>Lasers</td></tr>
<tr><td>Doxycycline (oral)[c]</td><td>Doxycycline (oral)[c]</td><td></td></tr>
<tr><td colspan="8">General skin care, SPF > 30, moisturizers, mild cleansers, avoidance of inciting factors.</td></tr>
<tr><td colspan="8">EPSOLAY Cream, 5% (benzoyl peroxide in silica-based), 5% has been FDA approved for the treatment of rosacea [8].</td></tr>
</table>

Table 3: Physical Modalities Used in the Treatment of Rosacea [9].

	Methods	**Treatable Symptoms**	**Recapitulative Assessment**
Light & Laser Therapies	PDL	Erythema, telangiectasia	More selective treatment of vessels compared to IPL. More efficient than Nd: YAG. Possible post-treatment purpura when using short-pulsed PDL. Possible hyper/hypopigmentation.
	KTP Laser	Telangiectasia (erythema)	Reduced healing times, more tolerable, lower risk of scarring, and better outcome of telangiectasia compared to erythema.
	Nd: YAG Laser	Erythema, telangiectasia	Risk of atrophic scarring
	IPL	Erythema, telangiectasia, papules/pustules	Good tolerability profile; it is time-saving
Surgical Options	Scalpel excision	Phyma	Intraoperative bleeding risk; Resection of additional tissue
	Dermabrasion	Phyma	Risk of bleeding
	Electrosurgery	Phyma	Possible side effects: cartilage necrosis, prolonged healing, atrophic
	Laser surgery (CO2 or erbium:YAG laser)	Phyma	CO2 lasers have a low risk of bleeding, Erbium: YAG lasers have a low risk of scarring, and they can be combined.

The 595 nm Flash-Lamp Pulsed Dye Laser (PDL) is still the mainstay of laser therapy in dermatology. It was developed according to the principles of selective photothermolysis and for the treatment of vascular lesions specifically. It remains the most common modality due to its proven safety and efficacy in port-wine stains, hemangiomas, facial telangiectasia, rosacea, and poikiloderma of Civatte [10].

PDL, in this regard, possesses high efficacy in reducing facial erythema, leading to an overall increased quality of life among patients suffering from rosacea. The laser targets the vascular lesions, including telangiectasia, selectively due to the preferential absorption of light by oxyhemoglobin. Equally important, the epidermal tissue around the site of treatment is also protected from the adverse effects due to the application of long pulse duration in relation to the integrated cooling mechanisms [11].

It enables coagulation of small vessels with effective fluences and multiple pulses at sub-purpuric fluences without the risk of rupture in the vessels. In addition, oxyhemoglobin has an absorption profile that allows for proper targeting of vascular malformations with the least insult to tissues in close proximity. In addition, post-treatment upregulation in transforming growth factor-beta 1 (TGF-β1), which is a cytokine regulating both the anti-inflammatory and the collagen synthesis pathways, has been reported. These immunomodulatory effects are critically important in PPR, in that they take into account the major pathogenic mechanisms. Transient erythema and/or purpura are common findings immediately post-PDL treatment; the normal course of these changes will usually be 7 to 10 days. Though rare, there have been reports of complications including hyperpigmentation, hypopigmentation, and even atrophic scarring, suggesting the need for careful selection of patients and close monitoring during the course of treatment [12].

Objective: This study aims to assess the safety and effectiveness of pulsed dye laser therapy in managing rosacea

Patients and method: A prospective interventional therapeutic study on fifty patients, 21 with papulopustular rosacea [PPR], and 29 with erythematotelangiectatic rosacea [ETTR] attending the outpatient dermatology clinic. Laser sessions in the study were given to the patients in a range of 2 to 6 sessions, and each was performed monthly. Before each treatment session, the facial skin of the patients was cleaned with soap and water. A careful examination of the skin of the face was done under good lightening conditions, and the determination of the skin phenotypes.

Researcher Scoring: [13] Condition of the patients was assessed in the treatment regimen by the scoring systems of Investigator Global Assessment (IGA) and Clinical Assessment Tool (CAT) for PPR and ETTR subtypes of Rosacea, respectively. It was assessed both before and after the treatment regimen. Details of the scoring for the Investigator Global Assessment are shown in Table 4.

Table 4: Rosacea Subtypes Investigator Global Assessment Scoring.

IGA		Definition	Guide line
0	Clear	The patient was asymptomatic	Skin completely free of any lesions indicative of inflammation
1	Near clear	One or two present, papules	1-2 small non-inflammatory papules
2	Mild	Find some papules/pust	Presence of 3-10
3	Moderate	Moderate number of papules/pustules	11-19 pap
4	Severe	Numerous papules/pustules, and nodules	More than 20 papules/pustules and nodules

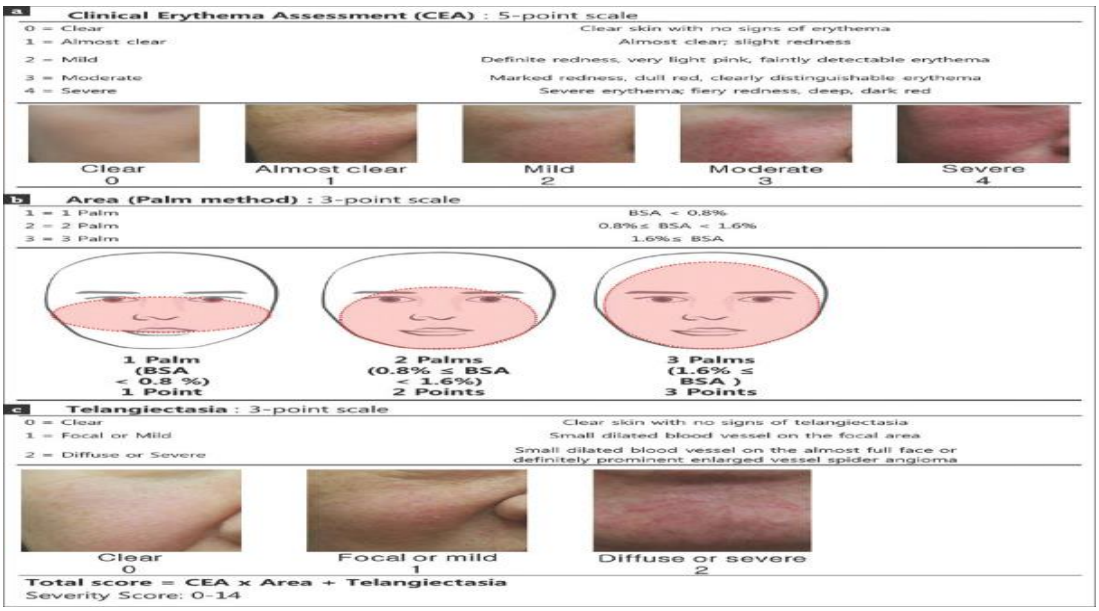

Fig. 1: CAT scale [14].

Treatment Protocol:

It is important that patients are clear of any leftover topical anesthesia before a laser procedure is performed. The patient's eyes need to be covered with protective spectacles or goggles that have filtering optics to ensure protection against dangerous laser light reflections or scatter, especially in the PDL wavelength. The spot size should be 7 mm, and the DCD should be set on a medium level (20/30). The pulse duration should be 3 ms for ETTR and 6 ms for PPR. Begin at an 8 J/cm^2 fluence and gradually increase up to a maximum of 11 J/cm^2.This can be used only when a handpiece is applied, touching perpendicularly to the skin surface, and it gives erythema for PPR or light purple for ETTR, respectively, to aim either to coagulate the blood vessels or to rupture them, according to the diameter of the blood vessel, which is in line with TRT of the blood vessels. Post-procedure, zinc oxide cream is applied, and the patient is advised to continue the daily application of zinc cream and be advised about irritants to avoid as far as possible. The patient is encouraged to use topical emollients daily and to avoid triggering factors like heat, alcohol, hot beverages, spicy food, and sun exposure as far as possible. A follow-up visit 4 weeks after each procedure, with advice to patients on sunblock application and monthly follow-up thereafter. The follow-up period extends to at least 3 months after the last session, with no relapses reported.

Socio-Demographic Profile: The mean age of the participants is 43.2 ± 9.8 years; the highest proportion is in the age group 40-49 years. A very large majority of the participants amount to 84% as females, and males constitute the balance 16% in this cohort. The mean duration of the disease is 3.7 ± 1.3 years among the participants.

Skin types: 74% of the participants mainly had type 3 skin, 20% had type 4, and only 6% had type 2 skin.

Triggering factors of rosacea: All participants (100%) indicated sunlight as a triggering factor of rosacea. Exposure to heat has been cited as the second-most, by 88% of the participants, while that of hot beverages, spicy food, and alcohol intake comprised 58%, 82%, and 2% respectively. Forty-four percent of the participants reported stress.

Treatment Parameters: Most common work joules selected were 8-9 J (32%), 8-10 J (32%), with lesser numbers selecting 8-10.5 J (12%), and 8.5-9.5 J (10%). Pulse diameter was most commonly 3-6 mm (56%) or 6 mm (42%) with 7 mm as a spot size; cooling was set at 20/30 for all participants (100%).

Type of rosacea: With respect to the type of rosacea, 29 participants (58%) have ETTR, while 21 participants (42%) have PPR.

Number of sessions: the average number of treatment sessions given in the study is 3.9 ± 1.6 sessions per patient. The most common related and required number of sessions were 2 sessions, 26% of cases, 6 sessions 22%, and 3 or 5 sessions, 20%. The least common were 4 sessions, 12% of cases, as presented in Figure 2.

There was no statistically significant difference in this with respect to the type of rosacea, P = 0.860.

The result of the laser sessions

The series of laser sessions had promising results. Patients of both the ETTR and PPR groups had better results for the treatment in the 20-month duration of the study. Paired samples t-test displayed was considerable difference, P = 0.000, as shown in **Table 5.**

Moreover, there was a significant difference at P=0.000 in treatment response between the two groups, based on calculated percent differences before and after treatment for each group, in which the PPR group achieved higher results, as shown in **Table 6**.

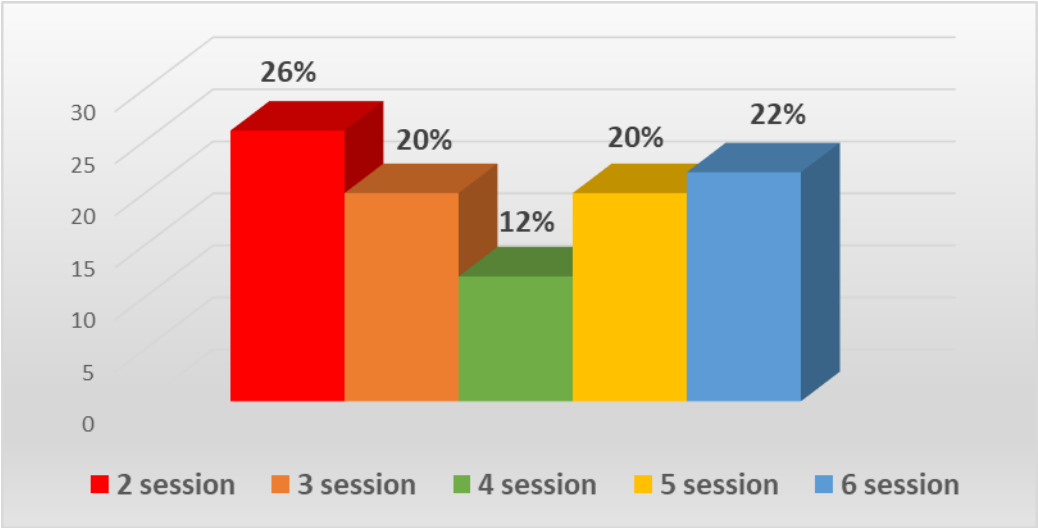

Fig. 2: Shows the distribution of the patients based on the attended session.

Table 5: Outcomes of two groups.

Variable	Before Tx.	After Tx.	Mean difference	t test	P value
	Mean±SD	Mean±SD	Mean±SD		
ETTR before tx.-ETTR after tx.	8.48	2.17	6.31	15.758	0.000*
PPR before tx.-PPR after tx.	3.33	0.71	2.62	4.093**	0.000*#

*Significant result **Z value #Wilcoxon signed ranks test used

Table 6: The difference between the two groups.

Variable	ETTR mean difference % (before/after)	PPR mean difference % (before/after)	Mean difference %	t test	P value
	Mean±SD	Mean±SD	Mean±SD		
ETTR mean diff.%-PPR mean diff. %	45.08±15.40	65.48±18.50	-20.40	-4.247	0.000*

*Significant result

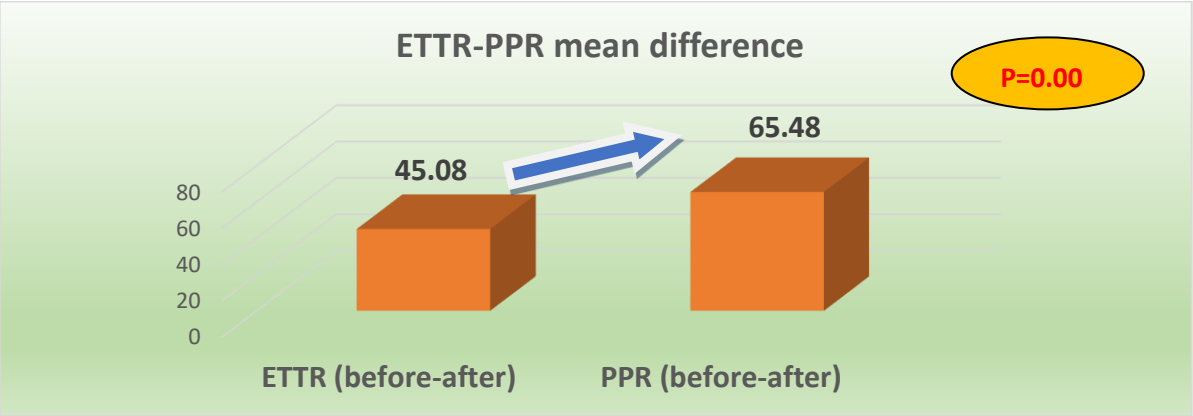

Fig. 3: displays how the participants reacted to the differences between the groups.

Fig. 4: 52-year-old female patient with PPR.

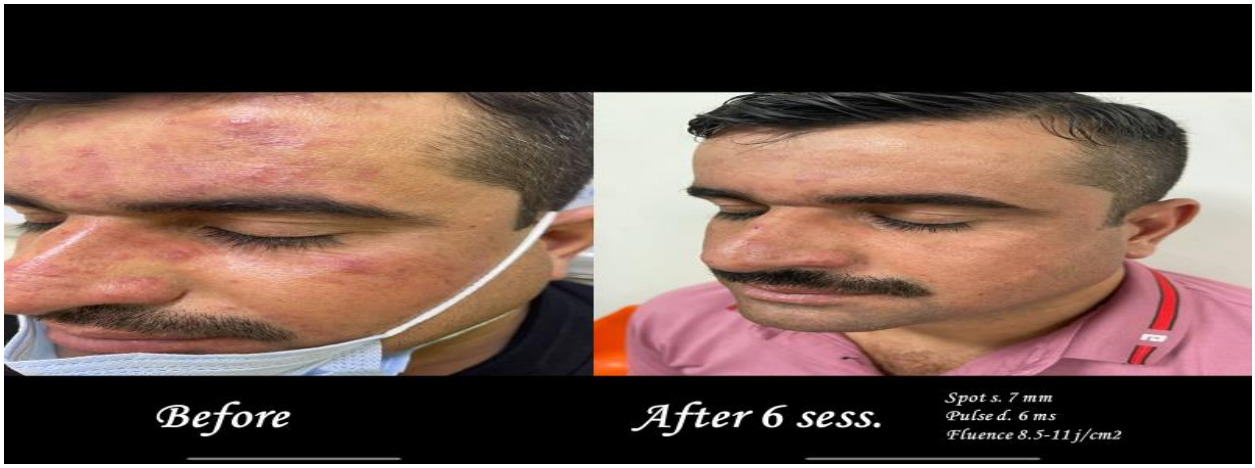

Fig. 5: 38-year-old male patient with PPR.

Fig. 6: 55-year-old female patient with PPR.

Fig. 7: 40-year-old female patient with ETTR.

Fig. 8: 27-year-old female patient with ETTR.

Fig. 9: 37-year-old female patient with ETTR.

Fig. 10: 40-year-old female patient with ETTR.

Discussion

The clinical features of rosacea have proven to be a challenge due to variability, which often includes telangiectasias and papular/pustular lesions, frequently unresponsive or not well controlled by medical therapy, particularly the erythematotelangiectatic subtype (15), the 595-nm pulsed dye laser (PDL) offers a breakthrough and is now considered a cornerstone in the management of the superficial blood vessels, which are the principal pathogenic lesion contributing to the prominent erythema in rosacea. More recent generations of PDL systems, characterized by longer pulse durations, higher energies, and integrated skin cooling mechanisms, have brought safer, nonpurpuric, and efficacious treatment modalities for the erythema and telangiectasia associated with rosacea (16).

The mechanism of action of PDL is based on the principle of selective photothermolysis [17]. In our study, we used a spot size of 7 mm and a fluence between 8 and 11 J/cm2, which is very similar to that used by Bulbul et al.: a median spot size of 7 mm (range 7–10 mm) and a median fluence of 8.5 J/cm^2 (range 8–12 J/cm^2). However, there was some variation in median pulse duration, with our study being 10 to 20 ms. There was significant improvement in both the erythema and telangiectasia scores after treatment ($p < 0.001$). The PCA analysis stated that nine of the patients showed clinical improvement of more than 50%, and 11 of the

patients reported good to excellent improvement. (15) PDL has proven efficacy in the treatment of rosacea, particularly PPR type, in previous studies. For example, Osman et al. demonstrated an increase in levels of TGF-β1, which is a cytokine related to anti-inflammation and the production of collagen after PDL application. It has an anti-angiogenic and anti-inflammatory effect on several pathogenic aspects of PPR [17]. The findings of Tan et al. were in agreement with our results when they treated forty patients with rosacea using a pulsed dye laser at a wavelength of 585 nm, a spot size of 5-7 mm, a pulse duration of 0.45 ms, and a fluence of 5-6.5 J/cm^2 with a 1 mm spot overlap. Post-laser treatment was performed after 1–10 sessions, and the mean scores of improvement were 4.4 and 4.3 for overall improvement. They showed marked improvement in symptoms of the disease and quality of life post-PDL therapy, with satisfaction expressed by patients towards the treatment outcome was reported [18]. Similar findings in many studies have also been reported by Bonsall et al., where they noted significant objective reductions in erythema scores of the rosacea patients in all facial regions ($p<0.01$), which reflect positively on the quality of their lives [20].

In the study by Strand et al., a visible tendency has been noticed with the increased numbers of treatment cycles from 2 up to 6: the efficacy of pulsed dye laser (PDL) treatment in rosacea sufferers remained statistically significant. The same tendency has been shown during the follow-up period, which took place three months after the last treatment cycle. More importantly, this study cited a positive relationship with repeated PDL treatments at the 595 nm wavelength of the V Beam Candela Perfecta® device and persistent improvement of symptoms associated with rosacea. Parameters used in treatment at baseline were a 10 mm spot size, with a fluence of 5 J/cm^2 and pulse duration of 10 ms. This regimen had a clinically meaningful improvement in 68% of the patient population [21].

These findings are in line with the conclusions drawn by Seo et al., who also studied the therapeutic efficacy and safety profile of PDL in managing rosacea. Utilizing a 585-nm long-pulsed PDL with specific parameters (fluence of 7 J/cm^2, spot size of 10 mm, and pulse duration of 6 ms), Seo et al. observed a statistically significant reduction in the index of erythema measured using spectrophotometry ($p < 0.001$). The congruence among these studies underpins the robustness of PDL as a viable treatment modality of rosacea, further reinforcing the clinical utility and the therapeutic value of PDL in dermatological practice [22].

Overall, the current investigation found no significant adverse reaction related to PDL except mild Adverse effects considered significant in this study, linked to the use of pulsed dye laser (PDL) discomfort, transient erythema, and mild purpura. The latter findings are in agreement with the literature. In general, such manifestations, which are most often met when applying PDL, including erythema, edema, purpura, and discomfort, are generally transient and nonsignificant. Although infrequent, hyperpigmentation was reported in a minor number of treated patients [22]. Our study showed a mean ± SD Epidermal to Total Tissue Ratio (ETTR) of 45.08±15.40, which translates to a significant improvement post-treatment. For comparison, Bernstein et al. reported a 53.9% ± 2.6% improvement in rosacea using PDL alone, with spot sizes of 15 mm and 3×10 mm, pulse duration of 3ms, and fluences of 6.25-7 J/cm^2 [23]. Similarly, Osman et al. demonstrated an improvement in the papular and pustular lesions by using PDL treatment at 585 nm, with spot sizes of 5-7 mm, pulse duration of 0.45 ms, and fluences of 5-6.5 J/cm^2, pre- and post-treatment having statistically significant differences (P=0.000) [17].

Noteworthy measures that can be used to reduce the development of purpura with PDL treatment include the use of sub-purpuric pulse durations and triple and

double pulses described by Mariethoz et al. with a 595 nm PDL at 6ms pulse duration and fluence of 4 to 6 J/cm^2 and a 10 mm spot size [19,24]. In addition, the use of pretreatment with lidocaine anesthesia, as in our study, was not found to compromise the result of PDL treatment. In fact, proper pain control in cosmetic procedures is very critical in making the patient more comfortable and satisfied with the service received.

Consistent with our findings, Elwan et al. reported statistically significant improvement in papulopustular rosacea (PPR) post-PDL therapy (p value = 0.005) [25]. We also found that a majority of the female patients in our study suffered from rosacea, which is also in consensus with Elwan et al., who showed that generally, women have elevated ferritin levels in rosacea. This may be because the skin in females is thinner than in males, thus becoming more susceptible to UVA-mediated damage. A dramatic downregulation of ferritin after treatment with PDL further emphasizes the use of PDL for the alleviation of photodamage and oxidative stress [25].

In a diagnostic investigation of rosacea, Tisma et al. reported a significantly increased number of ferritin-positive cells in affected skin samples, most intensely in cases of severe manifestation, vs. the controls ($P < 0.001$) [21]. The evidence collectively provides a clinical use for and effectiveness of PDL therapy in the treatment and management of rosacea with respect to both symptom and underlying pathophysiological process amelioration.

Conclusion:

It can be concluded based on our study that PDL is safe and effective in treating both papulopustular rosacea (PPR) and erythematotelangiectatic rosacea (ETTR), with excellent results seen more in cases of PPR. Tolerability was high, with only a few mild adverse effects reported.

Recommendation:

1. Caution should be exercised in using combined topical anesthesia, as the vasoconstrictive nature of these products could worsen the symptoms.
2. In PPR cases, adjunctive low-dose isotretinoin therapy in combination with PDL treatment should be considered.
3. Comparative studies are warranted to investigate efficacy more rigorously in comparison with other treatment options, including monotherapy with PDL and a combination of PDL with ivermectin cream or tablets.
4. IHC staining can be applied to research the levels of ferritin before and after treatment, which may serve as an additional clue toward the mechanistic underpinning of PDL therapy in managing rosacea.

Ethical Approval

Ethical approval was obtained for all samples, and patient consent was obtained under approval Center of Dermatology\ Baghdad Medical City, dated December 2023.

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Conflict of Interest

The authors declare and acknowledge that they have no conflict of interest.

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