ORIGINAL ARTICLE

CONTENTS

High-energy Nd: YAG laser therapy for papulopustular rosacea: Quantitative assessment with digital image processing

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ABSTRACT

Aim: To provide a quantitative assessment of the clinical effectiveness of the high-energy Nd:YAG laser therapy versa traditional pharmacotherapy in patients with papulopustular rosacea.

Materials and Methods: The study included 40 patients with clinically diagnosed papulopustular rosacea. Participants were divided into two subgroups: one received standard pharmacotherapy with systemic retinoids, and the other underwent fractional Nd:YAG 1064 nm laser treatment. Clinical outcomes were assessed using digital image analysis (ImageJ software), with erythema quantified in pixel units and relative facial area involvement. Statistical evaluation was performed with Student's t-test, considering $p < 0.05$ as significant.

Results: Both treatment modalities demonstrated clinical improvement; however, outcomes were more pronounced in the laser-treated group. Traditional pharmacotherapy achieved a 22% reduction in erythema area, while Nd:YAG laser therapy resulted in a 79% reduction. The proportion of erythematous facial area decreased from 24.4% to 16.7% in the pharmacotherapy group and from 27.6% to 5.7% in the laser group. No systemic or local adverse effects were reported.

Conclusions: Nd:YAG FRAC3® laser therapy demonstrated superior efficacy over pharmacotherapy in reducing erythema and inflammatory manifestations in papulopustular rosacea. These findings support its role as an effective and safe alternative or adjunct to standard pharmacological management.

KEY WORDS: papulopustular rosacea; Nd:YAG 1064 nm laser; erythema; digital image analysis; retinoids; laser therapy

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INTRODUCTION

Papulopustular rosacea (PPR) is a chronic inflammatory skin disorder marked by persistent facial erythema with papules and pustules, but without comedones as in acne vulgaris [1]. It usually develops between 30 and 50 years of age, is more common in women, and carries significant psychosocial impact [2, 3].

The pathogenesis involves dysregulated innate immunity, neurovascular reactivity, and alterations of the skin microbiome [3]. Overexpression of cathelicidin peptides, increased Demodex folliculorum density, and environmental triggers such as UV exposure and stress contribute to recurrent inflammation.

Standard therapy includes topical agents (ivermectin, azelaic acid, metronidazole), systemic antibiotics, and isotretinoin in resistant cases. Newer approaches—such as microencapsulated benzoyl peroxide, biologics targeting interleukin pathways, and Nd:YAG laser therapy—offer promising alternatives [4].

Despite therapeutic advances, PPR remains a relapsing condition that requires optimized, mechanism-based management strategies [5, 6].

AIM

The aim of the study is to evaluate the comparative effectiveness of standard pharmacotherapy and high-energy Nd:YAG 1064 nm (FRAC3 mode) laser therapy in patients with papulopustular rosacea, with objective assessment of erythema dynamics using digital image analysis..

MATERIALS AND METHODS

The clinical investigation was conducted on patients diagnosed with papulopustular rosacea (PPR). A total of 40 individuals were selected following comprehensive clinical, laboratory, and instrumental evaluations aimed at confirming the diagnosis and ruling out comorbidities or contraindications to systemic and laser-based therapies. All participants provided written informed consent regarding both treatment procedures and photographic documentation. The study cohort was balanced for age and sex distribution.

Inclusion in the PPR group required the presence of persistent centrofacial erythema accompanied by

Table 1. Baseline demographic and clinical characteristics of the study cohorts

Indicator, Unit of Measurement	Groups		
	PPR	PPR-Nd	$P_{PPR:PPR-Nd}$
Number, n	20	20	p > 0.05
Age, years	37±5.1	38±4.8	p > 0.05
Gender, males, n (%)	3 (15.0)	4 (20.0)	p > 0.05
TC, mmol/L	4.1 ± 0.82	4.1 ± 0.76	p > 0.05
LDL-C, mmol/L	2.36 ± 0.65	2.38 ± 0.60	p > 0.05
TG, mmol/L	3.85 ± 0.26	3.45 ± 0.24	p > 0.05
BMI, kg/m^2	22.5 ± 4.0	23.0 ± 4.21	p > 0.05
ESR, mm/hour	7.67 ± 3.2	5.8 ± 4.62	p > 0.05
D-dimer, ng/L	0.27 ± 0.12	0.26 ± 0.15	p > 0.05
SBP, mmHg	126.2±5.3	130.3±7.4	p > 0.05
HbA1c, %	4.5±0.62	5.0±0.68	p > 0.05
Glucose, mmol/L	4.8±0.87	5.0±0.82	p > 0.05
Hemoglobin, g/L	149.1±7.89	154.3±9.62	p > 0.05
Erythrocytes, 10^{12}/L	5.0±0.83	4.9±0.92	p > 0.05

Source: compiled by the authors of this study

Table 2. Comparative analysis of objective digital erythema parameters across patient groups

Groups	PPR	PPR-Nd	P
S, Pixels	96622.78 ± 83805.56	101022.2 ± 6295.77	p > 0.05
S_percentage_of affected_area, %	24.44 ± 20.33	27.68 ± 12.25	p > 0.05

Source: compiled by the authors of this study

Table 3. Variation in mean erythema surface area before and after one month of treatment in different study arms

Groups	S1, Pixels	S2, Pixels	ΔS, %	p
PPR	96622.78 ± 83805.56	65500.11 ± 6968.87	22.22	p < 0.05
PPR-Nd	101022.2 ± 6295.77	20944.4 ± 7556.78	79.10	p < 0.05

Source: compiled by the authors of this study

Table 4. Ratio of erythematous area to the overall facial surface: mean values across treatment groups

Groups	S_selected_area, Pixels	S1_percentage_of affected_area, %	S2_percentage_ofaffected_area,%	p
PPR	354268.22 ± 167526.69	24.44 ± 20.33	16.7 ± 10.2	p<0.05
PPR-Nd	386856.5 ± 124369.96	27.68 ± 12.25	5.72 ± 5.37	p<0.05

Source: compiled by the authors of this study

inflammatory papules, pustules, and localized edema. These features occurred against the background of vascular alterations characteristic of rosacea, differentiating the condition from acne vulgaris by the absence of comedones. Patients also reported subjective symptoms such as burning or stinging sensations. The diagnosis was established by a board-certified dermatologist based on standard clinical criteria.

Participants were stratified into two therapeutic subgroups:

Conventional pharmacological therapy (PPR group). Oral isotretinoin (Roaccutane, F. Hoffmann-La Roche, Switzerland) administered at 0.5–1.0 mg/kg body weight once daily. Dosage adjustments were made according to body weight and tolerability. Female participants of reproductive age were enrolled under the mandatory pregnancy prevention program.

Laser therapy (PPR-Nd group): High-energy Nd:YAG laser treatment (Fotona Dualis SP II, Slovenia) performed in fractional FRAC3 mode.

Objective assessment of treatment efficacy was performed through standardized digital photography under constant lighting and exposure conditions [7]. Image analysis was carried out using ImageJ software (version 1.54k, NIH, USA). Regions of interest (ROIs) were selected from affected facial zones. The erythema

Fig. 1. Digitalized representation of the erythematous zone in a patient with papulopustular rosacea
Picture taken by the authors

index was quantified by measuring the proportion and mean intensity of red pixels per square area (PPI – pixels per inch). Comparative analysis was conducted using pre-treatment and one-month post-treatment images.

Additional indices, including the red-to-green channel intensity ratio (R/G ratio), were calculated to provide a relative measure of vascular inflammation. Baseline laboratory tests were performed for all participants to exclude systemic comorbidities. These included complete blood count, lipid profile, fasting glucose, HbA1c, and D-dimer assays. Results were within reference ranges, confirming the localized inflammatory nature of the disease.

RESULTS

The assessment of therapeutic response in PPR was carried out by objective digital analysis of erythema severity [8]. Quantification was based on the measurement of red channel intensity within predetermined regions of interest (ROI) from standardized clinical photographs. A decline in red pixel intensity following treatment was interpreted as attenuation of the underlying inflammatory process.

To evaluate dynamic changes, a delta-percentage method was applied using the following equation:

$$\Delta = \left| \frac{[X_{fin} - X_{init}]}{X_{init}} \right| * 100$$

where Xfin represents the post-treatment value and Xinit is the baseline value.

Relative reduction of the erythematous surface area was determined by the formula:

$$\Delta S = \frac{S_1^{\square} - S_2}{S_1^{\square}} * 100\%$$

with S1 denoting the area of erythema prior to intervention and S2 the corresponding area after intervention.

Fig. 2. Sequential visual documentation illustrating changes in erythema extent in a PPR patient during therapy
Picture taken by the authors

Fig. 3. Quantitative digital assessment of erythema dynamics in a PPR patient, based on pixel analysis
Picture taken by the authors

Beyond mean values, additional insight was obtained by generating histograms of red channel distribution within selected ROIs. Therapeutic improvement was reflected by a leftward shift of the dominant peak toward lower intensity values, consistent with reduced erythema severity. Heat-map visualization, produced by applying LUT filters such as "Red Hot" in ImageJ, provided qualitative confirmation of the observed changes.

As a complementary index, the Red-to-Green ratio (R/G ratio) was computed to characterize the predominance of redness relative to the baseline skin tone. A decline in this parameter following treatment was indicative of progressive normalization of the cutaneous condition. All quantitative data are presented as mean ± standard deviation (M ± SD).

According to patient histories and clinical examination (Table 1), the first noticeable signs of papulopustular rosacea typically began as persistent erythema on the central face, most often on the cheeks, which subsequently extended to the upper and lower thirds of the facial region.

Unlike the erythematotelangiectatic form, the papulopustular subtype was consistently accompanied by inflammatory papules, pustules, and variable edema of the affected skin. In 83.3% of patients, the lesions recurred repeatedly, while one-third (33.3%) demon-

strated clear tissue infiltration. A smaller proportion (16.6%) also reported subjective symptoms such as itching, burning, or discomfort. The representative clinical appearance of these patients is illustrated in Fig. 1.

Quantitative image analysis confirmed the more pronounced inflammatory profile of PPR. The baseline erythematous surface area in patients from the PPR and PPR-Nd groups measured 96,622.78 ± 83,805.56 pixels and 101,022.2 ± 62,957.7 pixels, respectively (Table 2). An additional confirmatory parameter, the relative proportion of erythematous involvement to the total facial surface area (S_percentage_of_affected_area), averaged 24.44% ± 20.33 in the PPR group and 27.68% ± 12.25 in the PPR-Nd group. These values demonstrate the predominance of diffuse erythema combined with inflammatory elements in papulopustular rosacea.

In line with the study protocol, patients were allocated to different therapeutic strategies:

PPR group (pharmacotherapy): Received oral isotretinoin (Roaccutane, F. Hoffmann-La Roche, Switzerland) at a dosage of 0.5–1.0 mg/kg daily. Dosing was adjusted based on body weight and tolerability. In all patients, treatment was well tolerated, with no systemic or local adverse reactions and no cases of hypersensitivity to the active substance or excipients.

PPR-Nd group (laser therapy): Treated with Nd:YAG laser in FRAC3 fractional mode (1064 nm), applying both focal and diffuse regimens. Cooling was provided via Zimmer CRY06 or ice packs to minimize thermal discomfort.

Since erythema is the primary clinical hallmark of rosacea but lacks standardized clinical grading, digital image analysis was employed to objectively monitor treatment response. Standardized photographs were processed in ImageJ, allowing pixel-based quantification of erythema intensity and surface distribution (Fig. 2, Fig.3).

After one month of treatment, significant improvement was documented in both subgroups, though the magnitude of response differed. In the pharmacotherapy group, the mean erythematous area decreased by 22.22%, reflecting moderate but measurable improvement. In contrast, the laser-treated group (PPR-Nd) exhibited a far greater therapeutic effect, with an average reduction of 79.1% in erythematous surface area (Table 3).

To correct for potential anthropometric bias, an additional parameter was analyzed: the ratio of erythematous surface area to the total facial area. Both therapeutic modalities demonstrated statistically significant reductions (Table 4). In the PPR group, the ratio decreased from 24.44% ± 20.33 at baseline to 16.7% ± 10.2 post-treatment. In the PPR-Nd group, the same parameter declined from 27.68% ± 12.25 to 5.72% ± 5.37.

Collectively, these findings demonstrate that although conventional pharmacological therapy achieves partial improvement, high-energy Nd:YAG FRAC3 laser therapy produces a substantially more pronounced and rapid reduction in erythema and inflammatory lesions. Thus, Nd:YAG laser treatment may serve as a highly effective alternative or adjunct to systemic pharmacotherapy in patients with papulopustular rosacea.

DISCUSSION

Papulopustular rosacea (PPR) represents a chronic inflammatory phenotype of rosacea characterized by persistent erythema, papules, pustules, and localized edema. Conventional systemic therapy, such as isotretinoin or tetracycline derivatives, primarily targets sebaceous activity and inflammatory pathways, yet often provides only partial and delayed reduction of vascular symptoms [6]. In the present study, isotretinoin treatment produced a modest decrease in erythematous surface area (22%), confirming its limited efficacy against the persistent vascular component of PPR.

By contrast, Nd:YAG FRAC3 laser therapy achieved a substantial improvement, with an average erythema reduction of nearly 80%. The superior efficacy of Nd:YAG can be attributed to its deeper dermal penetration (1064 nm) and selective absorption by hemoglobin, allowing targeted coagulation of dilated vessels and attenuation of perivascular inflammation [9]. This dual effect not only diminishes background erythema but also facilitates regression of papules and pustules, aligning with prior reports that highlight the advantages of vascular laser therapy over pharmacologic interventions for inflammatory rosacea [10].

The strengths of this study include the use of digital imaging and quantitative pixel-based analysis, which minimized subjectivity and provided reproducible measures of erythema intensity and area. However, limitations should be acknowledged: the modest sample size and relatively short follow-up do not allow conclusions regarding long-term efficacy or recurrence.

Taken together, these findings support Nd:YAG FRAC3 laser therapy as a highly effective treatment for papulopustular rosacea, offering greater clinical benefit than systemic isotretinoin and representing a valuable adjunct or alternative within a comprehensive therapeutic strategy [10].

CONCLUSIONS

1. The application of digital image processing with ImageJ proved to be a valid and reproducible

method for objective quantification of erythema in papulopustular rosacea.
2. Systemic isotretinoin therapy resulted in a moderate improvement with a 22.2% reduction of erythematous area, while high-energy Nd:YAG 1064 nm FRAC3 laser therapy demonstrated superior efficacy, achieving a 79.1% reduction of erythema and marked regression of inflammatory lesions, confirming its role as an effective alternative or adjunct to pharmacotherapy.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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