Efficacy and safety of intense pulsed light in rosacea: A systematic review

Cintia Cristina Santi Martignago, Mirian Bonifacio, Laura Takahashi Ascimann, Patricia Gabrielli Vassão, Julia Risso Parisi, Ana Paula Renno, Livia Assis Garcia[1], Daniel Araki Ribeiro, Ana Claudia Muniz Renno

Department of Biosciences, Federal University of São Paulo - Unifesp, Silva Jardim, Santos, [1]Department of Biomedical Engineering, Institute of Science and Technology of Brazil University (UB), Rua Carolina Fonseca, São Paulo, Brazil

Abstract

Background: Rosacea is a chronic inflammatory disease of the skin characterised by facial erythema, oedema, telangiectasias, papules, pustules and nodules. There is a paucity of effective therapeutic modalities for the management of rosacea. Intense Pulsed Light (IPL), a modality in which flash lamps installed in an optical treatment device (head or tip) with mirrors to reflect light, has in recent times gained popularity in the management of this condition.

Aim: This systematic review aims to evaluate the efficacy, safety and adverse effects of IPL treatment for rosacea.

Methods: This systematic review was conducted in accordance with the Preferred Reporting Item for Systematic Reviews and Meta-Analysis. The electronic databases searched were Medline, PubMed and Scopus databases. The Risk of bias in non-randomised studies of interventions (ROBINS-I) and risk-of-bias tools for randomised trials (RoB-2) was employed to assess the risk of bias.

Results: Of a total of 233 articles retrieved from Medline, Scopus and PubMed databases, 14 studies qualified for final analysis. The studies included patients with Fitzpatrick skin types I to IV, with ages ranging from 15 to 78 years. Although the included studies showed heterogeneity between the parameters used, most studies demonstrated positive effects of IPL treatment on telangiectasia and erythema in rosacea and that the adverse effects presented were transitory.

Limitation: The methodological quality of the included studies was poor.

Conclusion: Although most studies showed the efficacy of IPL in the treatment of rosacea, the poor quality of the studies was of concern.

Key words: Intense pulsed light therapy, rosacea, systematic review, skin

Introduction

Rosacea is a chronic inflammatory cutaneous disorder affecting the face, especially the cheeks, chin, nose and forehead.[1,2] Cutaneous signs of rosacea include flushing, erythema, telangiectasia, oedema, papules, pustules and rhinophyma.[3] More than 50% of patients with rosacea also experience ocular symptoms such as dryness, irritation, blepharitis, conjunctivitis, and compromised vision.[4] It is more common in women and its prevalence varies across populations, ranging from less than 1% to 22%.[5]

The pathophysiological mechanisms of rosacea are unclear, but they involve genetic factors, vascular and neural abnormalities, dermal matrix degeneration, microorganisms and environmental factors, such as heat, nutrition and ultraviolet light.[2,6] The inflammatory process in the skin may

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Corresponding author: Dr. Cintia Cristina Santi Martignago, Department of Biosciences, Federal University of São Paulo - Unifesp, Silva Jardim, Santos, Brazil. csantimartignago@yahoo.com.br

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be worsened by pro-inflammatory substances and degradative enzymes released by inflammatory cells, leading to dermal destruction.[7]

The primary focus of rosacea treatment is to alleviate symptoms and improve facial appearance. Educating patients about their skin condition and potential exacerbating factors is an important aspect of management. This helps them identify and avoid triggers that can worsen their condition.[3,8] Beta-blockers, α2-adrenergic agonists and brimonidine tartrate are frequently used pharmacological interventions.[3,7,9]

Various light-based therapies such as low laser therapy and intense pulsed light (IPL) have been used for treating the erythema and telangiectasia of rosacea.[8,3] IPL uses non-collimated, non-coherent light of different wavelengths to target specific chromophores making it a versatile therapy for hair removal, skin rejuvenation and the treatment of pigmented or vascular lesions.[10] The 577 nm wavelength of IPL corresponding to the third absorption peak of oxyhaemoglobin is absorbed by haemoglobin inducing photothermolysis. This selectively destroys blood vessels and causes thermal damage to the papillary and upper reticular dermis.[11,12] IPL destroys abnormal vessels in patients with rosacea and improves the dermal connective tissue disorganisation of the vascular component of rosacea (erythema and telangiectasia).[13,14]

While the positive effects of IPL in treating rosacea are well-documented, its use is still controversial, particularly with regard to the parameters required to achieve optimal results. Despite advances in research on the use of light for managing rosacea, no systematic review of the exclusive use of IPL in rosacea has been conducted. The present study aimed to analyse literature on the effects and safety of IPL for treating rosacea-related symptoms in clinical studies.

Materials and Methods

This systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[15] at the Federal University of the State of São Paulo, Brazil in October 2022. It was registered on the online International Prospective Register of Systematic Reviews (PROSPERO) of the National Institute for Health Research (Registration ID: CRD42021285751).

We used the Medline, PubMed and Scopus electronic databases to systematically search for articles on IPL and rosacea in clinical trial studies. The Medical Subject Headings (MeSH) terms and Boolean operator in the electronic search strategy were “intense pulsed light” and “rosacea”. Articles were selected based on their titles and abstracts meeting the eligibility criteria. The methodological quality of all included studies was assessed using the Cochrane Risk of Bias (RoB 2.0)[16] scale for randomised clinical trials and Risk of Bias in Non-randomised Studies of Interventions (ROBINS-I).[17]

Inclusion criteria

We included only complete trials conducted in patients with rosacea and published in English. No publication date or publication status restrictions were imposed. The presence or absence of a control group (a group without treatment, a placebo IPL or a group with a different treatment modality) did not influence selection. Digital photographs in the articles were also evaluated.

Exclusion criteria

We excluded *in vivo* and *in vitro* studies, systematic reviews and meta-analyses, case reports and experimental studies, studies that used other interventions besides IPL, follow-ups of previously published trials and conference abstracts.

Outcomes Assessment

Data was extracted from the studies by two reviewers (ACMR and CCSM), who independently analysed the title and abstract. The selection was based on the inclusion and exclusion criteria and all differences were solved through discussion.

The study database included:

- Basic characteristics of qualified studies
- Characteristics of the subjects (number of participants, age, gender, etc.)
- Interventions (treated group, control group, or other treatment group and analyses)
- Details of the IPL used (spot size, mode, wavelength (λ), pulse rate, energy density and application area)
- Outcome measures that included the level of symptom improvement evaluated before and after treatment

Adverse effects were also assessed.

Results

The flow diagram shown in Figure 1 illustrates the search strategy used in the study. A total of 233 articles were retrieved from the Scopus and PubMed databases (147 and 86 articles, respectively). After excluding 64 duplicated records, 134 articles were excluded after reading the title and 8 after reading the abstract. The remaining 27 full-text articles were assessed for eligibility and finally 14 studies were selected for the systematic review. The classification of rosacea was not a criterion for the inclusion/exclusion of studies.

The general characteristics of patients and experimental groups from these 14 articles are summarised in Table 1. The studies included patients with Fitzpatrick skin types I to IV, with ages ranging from 15 to 78 years. Three studies recruited only females.[18,19,20] While 11 studies recruted both male and female patients.[12,13,21–29]

All studies used IPL alone as an intervention group. Ten studies did include any control groups.[13,18–20,23–28] three studies[12,20,28] used a group of pulsed dye laser (PDL) treated patients and 1 study used untreated patients as controls.[29] In

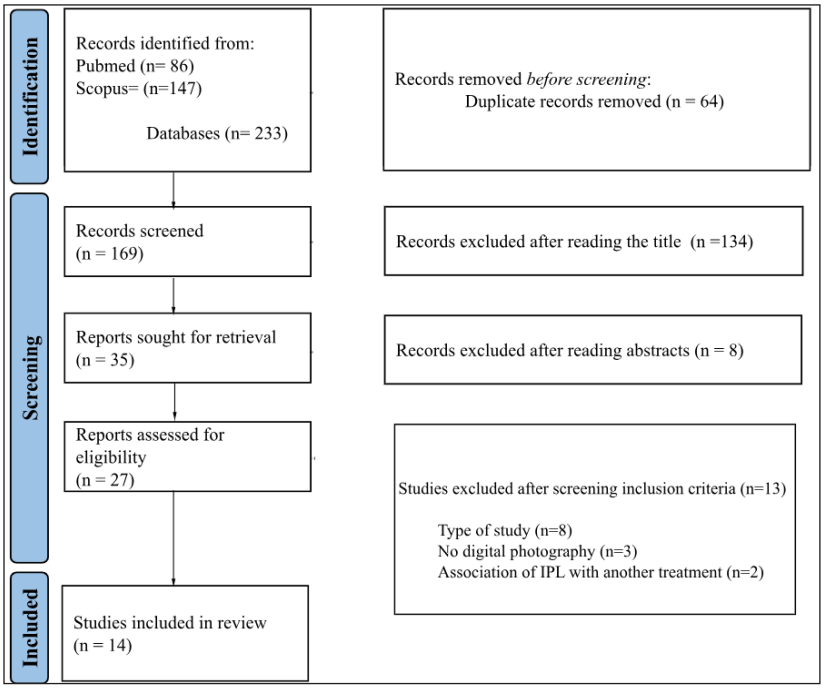

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of the studies included in the systematic review.

Table 1: General characteristics of patients and experimental groups

Authors	Number of participants/Gender	Age (years)	Skin type	Intervention group	Control or other treatment group	Study design
Mark *et al.*[18]	4 (female)	43 to 55	*	5 sessions every 3 weeks with the IPL	&	Case series
Schroeter *et al.*[23]	60 (55 female and 5 male)	Mean age of 44.2	Fitzpatrick I–IV	1 session of IPL (reevaluation after 1, 2, 4 and 12 weeks)	&	Case series
Kawana *et al.*[19]	6 (female)	37 to 66	Fitzpatrick skin type III	3 sessions of IPL (interval of 4 weeks)	&	Case series
Papageorgiou *et al.*[24]	34 (25 female and 9 male)	Mean age of 47 (18–65)	Fitzpatrick skin type I–IV	4 sessions of IPL (interval of 3 weeks)	&	Case series
Neuhaus *et al.*[29]	30 (20 female and 9 male)	Mean age of 45.8	Fitzpatrick skin types I–III	3 sessions of IPL (interval of 4 weeks)	4 patients received Pulsed Dye Laser to one side of the face and no treatment to the other side (control)	Clinical Trial
Campolmi *et al.*[25]	85 (64 female and 21 male)	28 to 75	Fitzpatrick skin types I–IV	5 sessions of IPL (range 4–6) at 3-weekly intervals	&	Case series
Kassir *et al.*[26]	102 (94 female and 8 male)	15 to 69	Fitzpatrick skin types I–IV	7 sessions (interval of 1-3 weeks)	&	Case series
Liu *et al.*[13]	32 (6 female and 8 male)	18–47 (median, 35.8)	Fitzpatrick skin phototype III–V	3 sessions (3-week intervals)	&	Case series
Lim *et al.*[27]	50 (male and female)	50.17	*	4 sessions (interval of 3 weeks)	&	Case series
Marques *et al.*[28]	9 (female and male)	36 to 59	Fitzpatrick skin types I to III	3 sessions (interval of 30 days)	&	Case series
Kim *et al.*[21]	9 (female and male)	20 to 59	Fitzpatrick skin types II–IV	4 sessions with an interval of 4 weeks(evaluation period baseline and at weeks 3, 6, 9, 12, and 15)	Pulsed dye laser	Clinical Trial
Tsunoda *et al.*[20]	13 (female)	36 to 78	*	4 sessions of IPL with an interval of 4-16 weeks	&	Case series
Luo *et al.*[22]	260 (female and male)	18 to 60	Fitzpatrick skin types III to IV	3 sessions of IPL with an interval of 4 weeks	Control group with no treatment	Clinical Trial
Tirico *et al.*[12]	5 (4 female and 1 male)	48 to 61	Fitzpatrick skin types I to III	2 sessions of IPL (patient's face was divided into left and right sides)	Pulsed dye laser	Clinical Trial

IPL: Intensed Pulsed Light; * data not described in the study; &: Only one treatment group

Table 2: Protocols and parameters of IPL used by the studies

Authors	Spot size	Pulse duration	Wavelength (nm)	Energy density
Mark *et al*.[18]	*	a single pulse duration of 3 ms	515	22 and 25 J/cm^2
Schroeter *et al*.[23]	8 × 35 mm^2	4.3 and 6.5 ms	515 to 1.200	15 and 90 J/cm^2
Kawana *et al*.[19]	10 × 15mm^2	20 ms	550–670	21 J/cm^2
Papageorgiou *et al*.[24]	34 × 8 mm^2	15 ms	560	24–32 J/cm2
Neuhaus *et al*.[29]	*	6 ms	560	25 J/cm^2 (increase of 1 J/cm^2 at each subsequent session)
Campolmi *et al*.[25]	*	Double pulse of 3 to 8 ms	500 to 550	9 to 13 J/cm^2
Kassir *et al*.[26]	10 × 40 mm^2	2.5 to 5 ms	420–530	25 J/cm^2 for skin type 1, 21 J/ cm^2 for skin type 2, 17 J/cm^2 for skin type 3, 13 J/cm^2 for skin type 4, 10 J/cm^2 for skin type 5.
Liu *et al*.[13]	6.4cm^2	12 msec	540	10–12 J/cm
Lim *et al*.[27]	*	6-7 ms	560	12~16 J/cm^2
Marques *et al*.[28]	*	12 and 25 ms	535–680 and 860–1,200	10 to 20 J/cm^2
Kim *et al*.[21]	7 mm	1.5 ms	555	8 J/cm^2
Tsunoda *et al*.[20]	Two devices: 4 × 1 mm^2 and 6.35-mm mm^2	*	590–1200 wavelength and 500–635	22–24 J/cm^2 and 14–15 J/cm^2
Luo *et al*.[22]	1.5 × 4 cm^2	12 ms	540	10–16 J/cm^2
Tirico *et al*.[12]	10 × 48 mm	1.5 ms	595	4 J/cm^2 (with an increase of 0.5 J/cm^2 per section)

* data not available in the article

the study conducted by Neuhaus *et al.,*[29] patients were treated with IPL on one side of the face and PDL on the other.[29]

The IPL protocols used in the studies are detailed in Table 2. Spot sizes were mentioned in 7 studies and varied from 1 × 4 mm to 15 × 40 mm.[19,20,22–24,26,28] The pulse duration was specified in all studies and varied from 1.5 to 25 ms and the wavelengths used ranged from 420 to 1200 nm. In 4 studies, 2 separate handpieces emitting different wavelengths were used [Table 2].[20,23,27] The energy density applied also varied widely from 15 J/cm^2 to 90 J/cm^2.

Various evaluation methods were employed to assess the effects of IPL [Table 3]. All studies used digital photography to assess the area of telangiectasia, erythema, and the number of lesions.[12,18,20–23,25,26,28,29] Blood flow analysis was used in one study,[18] while two studies used spectrophotometer analysis.[19,29] Questionnaires and scales employed in these studies included various visual analogue scales (4, 5, 6, and 10 point VAS) and patient global assessment (PGA).

The positive effects of IPL persisted after treatment in all the studies. The area of telangiectasia and erythema as well as the number of lesions were significantly reduced after treatment.[18,20–26,28,29] Kassir *et al*.[26] observed that 80% of patients had reduced redness, 78% noted reduced flushing and improved skin texture, 72% reported fewer acneiform breakouts, and 51% demonstrated a reduction in telangiectasias. Tirico *et al*.[12] noted decreased redness after IPL treatment, Marques *et al*.[28] observed improvement in flushing and skin texture and Kim *et al*.[21] observed clinical improvement in erythema, telangiectasia, papules, and pustules. Improvement after IPL treatment was demonstrated by spectrophotometer analysis in two studies.[19,29]

Improvement in signs and symptoms after IPL treatment were confirmed through the use of scales and questionnaires. In the study of Campolmi *et al.*[25] Neuhaus *et al.*[29] noted an improvement in patient-rated signs and symptoms.

Adverse effects were transitory and included pain, oedema, minimal bruising, and burning sensations.

The risk of bias assessment for both the randomised and non-randomised trials is illustrated in Figures 2a and 2b. The RoB-2 assessment [Figure 2a] revealed an unclear risk of bias in all studies due to missing outcome data. This arose from the randomisation process in 3 studies and in the measurement of the outcome in one study. A high risk of bias was noted in one study due to deviations from intended interventions[29] and in 2 studies in the bias domain in selecting the reported result.[12,21] A low risk of bias arising from the randomisation process was noted in a single study,[29] in 2 in the selection of the reported result,[22,29] and in 3 studies each due to the deviations from intended interventions[12,21,22] or in the measurement of the outcome.[21,22,29]

In the ROBINS-I assessment [Figure 2b], one study had a high risk of bias in the field of measurement of outcomes.[26] Additionally, an unclear risk of bias was found in the domains of deviations from intended interventions,[26] missing data,[24] and measurement of outcomes.[23] All studies had a low risk of bias classification in the domains of confounding, selection of participants, type of interventions, and selection of the reported result.

Discussion

IPL is an effective non-invasive therapeutic intervention for the treatment of port wine stains, haemangiomas, and facial telangiectasia.[30,31,32] It has also been demonstrated to reduce

Table 3: Results after the intervention, outcomes and adverse effects

Authors	Evaluations	Results	Outcomes	Adverse effects
Mark *et al.*[18]	Blood flow and digital photographs (telangiectasia area and erythema colour).	- 30% decrease in blood flow; - There was a decrease of 29% in the area of telangiectasia and a 21% decrease in the intensity of erythema.	+	*
Schroeter *et al.*[23]	Digital photographs analysing facial clearance of telangiectasia and lesions on the forehead.	77.8% clearance of facial telangiectasia. 87% demonstrated clearance of the lesions on the forehead.	+	Erythema and purpure. Some patients complained of pain and oedema.
Kawana *et al.*[19]	Measurement of skin colour by spectrophotometer; Self-efficacy evaluation.	Improved values for spectrophotometer analysis and improved index of self-satisfaction.	+	Mild erythema in the same patients but disappeared several days later—some complaints of weak pain.
Papageorgiou *et al.*[24]	Colour digital photographs of the face; 10-point VAS (severity of erythema and severity of telangiectasia). Patients and doctor's assessments of rosacea using a six-point VAS.	The erythema reduction was 39% on the cheeks and 22% on the chin. Erythema improved by 46% and telangiectasia by 55%—reducing the severity of rosacea. The patient self-reported improvement of rosacea and reported a reduction of their flushing.	+	Side effects were minimal (bruising).
Neuhaus *et al.*[29]	Full-face digital photographs; Spectrophotometer of overall erythema grade and telangiectasia grade on a 4-point scale; quantitative telangiectasia counts of the face.	- No improvements in erythema in the malar region but an improvement in the cheek region. - Reductions in erythema Score. - Lower erythema and telangiectasia grade. - The reduced value of telangiectasia counts.	+	*
Campolmi *et al.*[25]	Photographs of the lesions; Clinical observations; Patient's subjective evaluation; Anthology-system photographs.	- All patients observed global improvements in their lesions; - 72 (80.9%) lesions achieved a marked improvement, 14 (15.7%) lesions a moderate improvement and 3.4%, a slight improvement. - 69 (81.2%) patients were very satisfied, 14 (16.5%) patients were satisfied and 2 (2.3%) patients were not satisfied.	+	Erythema, edema, swelling, mild purpura and pain.
Kassir *et al.*[26]	Digital photograph to measure redness, flushing, acne and telangiectasia.	80% of patients had reduced redness, 78% noted reduced flushing and improved skin texture, and 72% reported fewer acneiform breakouts. Photo Documentation showed a 51% reduction in telangiectasias.	+	*
Liu *et al.*[13]	Digital photographs Severity of erythema; Patient's satisfaction (10-point visual scale)	All patients showed clinical improvements and higher satisfaction after the treatment.	+	No noticeable side effects, except for transient erythema/oedema with resolution within a few days.
Lim *et al.*[27]	Rosacea severity; Physician's global assessment and patient's global assessment (4-point scale).	Significant differences in severity scores between pre-treatment and post-treatment were significantly observed.	+	Four patients complained of erythema, six pain during treatment, and one hyperpigmentation.
Marques *et al.*[28]	Digital photographs; Questionnaire to assess the treatment's efficacy using a scale; flushing, persistent erythema and telangiectasia.	Improvements in erythema and telangiectasia Significant improvement in skin texture and flushing; 50% were classified as having had more than 75% improvement in the overall clinical picture.	+	Burning sensation was reported by 50% of patients.
Kim *et al.*[21]	Photographic for evaluating erythema and melanin indices; Changes in investigator's Global Assessment (IGA); Subjective patient global assessment.	- Improvement of erythema and melanin indices; - Clinical improvement in erythema, telangiectasia and papules and pustules; - Improved values of IGA; - Clinical improvement of > 50% clearance; - 77.8% of patients reported being very satisfied or satisfied.	+	Transient erythema and oedema (symptoms resolved within a few hours without special management).
Tsunoda *et al.*[20]	Photographic assessments of facial telangiectasia used for quantitative evaluation; Clinical photographic a 4-point scale.	Improvement of the clearance of telangiectasia on the face.	+	*
Luo *et al.*[22]	Photographs allow the measurement of the severity of telangiectasia.	- 1 month after the initial IPL treatment, 19 (17.8%) patients with facial telangiectasia were characterised as improved. At 3 months, the total efficacy rate had increased to 39.2%; - 4 months, 72 (67.3%) patients showed some degree of improvement, while 35 (32.7%) patients showed effective treatment. - 6 months, 102 (95.3%) patients showed improvement, whereas 71 (66.4%) patients were effective.	+	Mild burning sensation, temporary skin flushing and local skin oedema faded spontaneously.
Tirico *et al.*[12]	Digital photographs.	Redness was reduced by an average of 60% on the IPL side and 45% on the PDL side.	*	Modest pain.

IPL: Intense Pulsed Light; PDL: Pulsed dye Laser; VAS: Visual Analogue Scale; *data not available in the article; +positive results for the outcomes evaluated

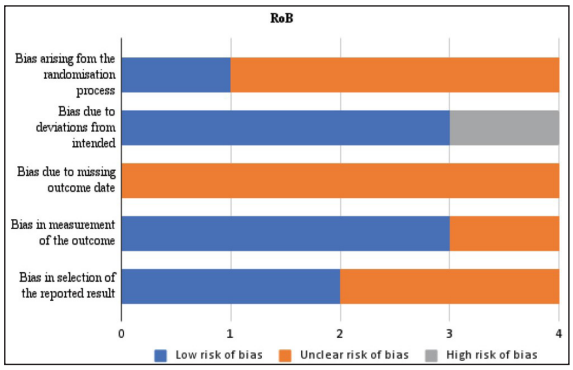

Figure 2a: Risk of bias assessment for the randomised clinical trials (RoB-2).

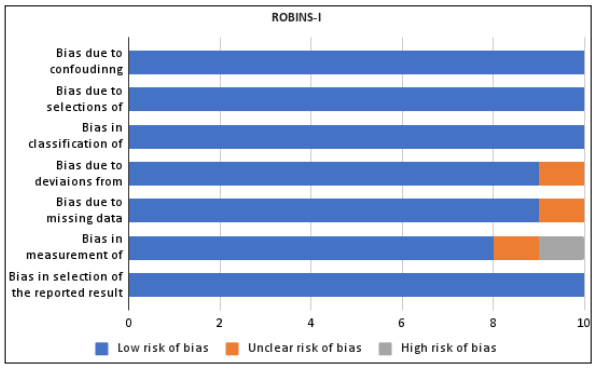

Figure 2b: Risk of bias assessment for the non-randomised intervention studies (ROBINS-I).

erythema, papules and pustules and improve skin texture in patients with rosacea.[33,34] Multiple sessions (up to 15) at 1-to-3-week intervals may be necessary, and parameters need to be adjusted individually according to the phototype, severity and tolerance to minimise side effects.[26]

Our systematic review found that IPL was effective in managing the symptoms of rosacea in both males and females of Fitzpatrick skin types I to IV aged between 15 and 78 years. However, due to the wide range of IPL parameters used in these studies (wavelengths varying from 420 nm[26] to 1200 nm,[23] energy density from 15 J/cm^2 to 90 J/cm^2,[23] and number of sessions from 1 to 7)[23,26], and the different methods used to evaluate the effects of IPL (digital photos, patient self-reported perception, scales, and questionnaires), the end results are not strictly comparable.

The optimal use of IPL parameters such as fluence, pulse duration, wavelengths, treatment time, and spot size in clinical settings is crucial for achieving the best tissue responses and minimising the risk of tissue damage.[31,35] Shorter wavelengths (400 to 585 nm) and shorter pulse durations (450 ms) are thought to have a better effect on skin owing to the limited depth of penetration (up to 1.5 mm).[33]

Papagerogiu *et al*, using a 560 nm a wavelength observed an average reduction of 3.5 points in the severity of rosacea pain measured with the 10-point VAS.[24] In this same study, over 50% improvement was seen in 73% and 83% of patients as per the evaluation of the patients and physicians respectively. The results were sustained for 6 months. Other authors used higher wavelengths (e.g., 1200 nm) and also noted good results.[30] These effects may be due to the absorption of wavelengths in the 900 to 1200 nm spectrum by water in the dermis triggering a cytokine reaction that stimulates the formation of elastin and collagens I and III.

A wide range of energy densities (from 15 J/cm^2 to 90 J/cm^2) were used in the studies. High energy densities can cause burns, while lower fluences may not be effective.[36] The spot size (area covered by the beam at the tip of the applicator) varied significantly among different machines, ranging from 4 to 64 mm^2.[20,28,37] The number of treatment sessions and the period of treatment were not uniform across the studies and between 1 and 7 treatment sessions at intervals of 3 to 4 weeks were used. Although standard IPL protocols suggest a 3–4 week interval between treatments, Papageorgiou *et al*. have proposed that a longer interval of 6 or 8 weeks may be more cost-effective.[24]

Most studies have reported an improvement in erythema and telangiectasia after IPL application.[30,38–44] This may be due to the ablation of abnormally dilated vessels and the reduction of extravascular leakage of inflammatory mediators.[13] IPL also stimulates new collagen deposition and collagen remodelling, which improves support for small blood vessels, dermal connective tissue disorganisation, and elastosis.[23,24] The improvement in the vascular features of rosacea (erythema and telangiectasia) could subsequently lead to a decrease in inflammatory lesions.[23,24,32]

Limitations

Eight of the studies were of low methodological quality.[18,19,23–28] Neither the investigators nor the subjects were blinded, and the treatments were not concealed.

Conclusion

IPL is a safe and effective treatment for rosacea. However, since all trials included in the studies show methodological limitations, more trials of better methodological quality must be conducted.

Declaration of patient consent

Patient's consent not is required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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