pISSN 0898-5901 | eISSN 1884-7269
Indexed in Scopus

Volume 30 - N. 2 - April 2023

Adverse effects associated with ablative lasers when treating common dermatologic conditions: a systematic review of 946 patients

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ABSTRACT

CO2 and Er:YAG are the two most common types of ablative lasers in use today. Ablative lasers are known for their superior efficacy in penetrating deeper through the skin layers when compared to non-ablative lasers. This review compares the outcomes and adverse events associated with CO2 and Er: YAG lasers, in conjunction with other therapeutic modalities, in the treatment of common skin conditions. A PRISMA-compliant systematic review of PubMed and Embase databases was conducted from January 2012 to December 2022. Study types that were eligible for this review included clinical trials, randomized controlled trials, case reports, case series, cohort studies, and meta-analyses. The study protocol was registered (PROSPERO 2022: CRD42022348569). The search strategy produced 27 studies comprising 946 patients who were treated for acne scars, postacne hyperpigmentation, solar lentigines, facial rejuvenation, refractory vitiligo, and epidermal verrucous nevi. Erythema, pain, and hyperpigmentation were the most commonly reported adverse effects. A higher rate of adverse events was observed in CO2 laser therapies (n=610, 64.5%) when compared to Er: YAG and other laser cohorts (n=40, 4.2%). Both CO2 and Er: YAG lasers demonstrate similar efficacy in the treatment of benign cutaneous conditions. Further research is needed for parallel comparison of CO2 and Er: YAG lasers.

Key words: CO2; Erbium:YAG; ablative; non-ablative; systematic review.

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Received: 26 November 2023.
Accepted: 4 December 2023.

Laser Therapy

Laser Therapy 2023; 30:378
doi:10.4081/ltj.2023.378

Introduction

Laser resurfacing is a rejuvenation procedure that uses both ablative and non-ablative lasers to treat cutaneous lesions, scars, skin tone, and texture in addition to reducing signs of photodamage and aging.[1] While ablative lasers use thermal energy to remove both the epidermal and superficial dermal layers of the skin to stimulate collagen production, non-ablative lasers yield less clinically significant results by exerting their effect on the dermis alone and sparing the epidermis.[1] Both the carbon dioxide (CO2) and erbium-doped yttrium aluminum garnet (Er:YAG) lasers emit energy in the infrared spectrum, which when absorbed by intracellular water, creates rapid heating and vaporization of local tissue.[2] Ablative lasers can be further subdivided into full-ablative and fractional ablative. Full-ablative lasers target the entire field of skin, whereas treatment of specific fractions or columns of skin within a localized area calls for "fractionated ablation".[3] In general, ablative lasers are best known for treating deeper lines, wrinkles, scars, discoloration, and pigmentary disorders because of their ability to penetrate through deeper layers of the skin. Ablative fractional resurfacing is also recommended for the treatment of textural skin changes associated with various cutaneous conditions, including involuted infantile hemangiomas.[4]

In addition to prolonged recovery time, ablative lasers are associated with the potential for infection, scarring, and pigmentary disorders, making them a less-than-ideal treatment for some conditions.[4] Between CO2 and Er:YAG lasers, the latter has a lower downtime post-treatment.[4] The risk for adverse effects with ablative lasers is greater in children who have fewer appendageal structures, including sweat glands and the pilosebaceous unit of the skin, as they are necessary for repopulating the ablated tissue.[4] Ablative fractional CO2 lasers are considered quite effective for the treatment of acne scars, however, treatment session, duration, and parameters should be tailored precisely for each patient. Combination therapy is generally recommended for ice-pick-type acne scars.[5] For chronic plaque psoriasis, laser treatment options range from CO2 to Er:YAG to pulsed dye to 1302 nanometer (nm) Nd:YAG and excimer lasers, although the efficacy and safety profile of 308 nm excimer laser has proven to be far superior to the rest of the laser modalities.[6]

The cost of Er:YAG and fractional CO2 are comparable, ranging from $300 to $1000 per session. In general, the fractional CO2 laser is a more versatile ablation therapy that enables the treatment of a wider spectrum of skin problems rather effectively. Erbium is a good alternative for treating hyperpigmentation in patients with darker skin types due to less risk of side effects.[7] In this review, we explore the role of both CO2 and Er:YAG lasers in treating common benign skin conditions such as acne, vitiligo, hyperpigmentation, and atrophic scarring. We also compare and contrast the therapeutic outcomes, complications, and adverse effects observed with the use of each kind of ablative laser when used with or without adjunct treatment modalities.

Materials and Methods

Study strategy and selection

A comprehensive literature search was conducted using PubMed and Embase databases (between January 2012 and December 2022) to identify relevant articles using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (2022). The initial search was performed during December 2023, after which the titles and abstracts were screened in January 2023 for inclusion criteria by three independent reviewers (E.R., E.D., O.E.). Full texts of shortlisted articles were then reviewed by three reviewers (E.R., E.D., O.E.) to ensure they met the inclusion criteria. Any disagreements were resolved by a fourth reviewer, H.G. Additional relevant articles were included from the bibliography of selected articles found during our database searches. Following that, pertinent variables such as type of study, type of ablative laser used, patient demographics, cutaneous lesion treatment, complications and adverse events resulting from the treatment, and patient satisfaction were extracted from each study. Study types that were eligible for this review included clinical trials, randomized controlled trials, case reports, case series, cohort studies, and meta-analyses. The study protocol was registered with the International Prospective Register of systematic reviews (PROSPERO 2022: CRD42022348569).

Search criteria

Combinations of search terms were run in both databases. We used the following search string to identify relevant articles:

PubMed
('skin lesion' AND 'complication' AND 'efficacy' AND ('erbium YAG laser' OR 'carbon dioxide laser'): 26 results ('acne scar' AND ('hyperpigmentation' OR 'hypopigmentation') AND ('erbium YAG laser' OR 'carbon dioxide laser') AND ('adverse event' OR 'outcome' OR 'complication'): 71 results

Embase
('skin lesion' AND 'complication' AND 'efficacy' AND ('erbium YAG laser' OR 'carbon dioxide laser'): 11 results ('acne scar' AND ('hyperpigmentation' OR 'hypopigmentation') AND ('erbium YAG laser' OR 'carbon dioxide laser') AND ('adverse event' OR 'outcome' OR 'complication'): 28 results

Inclusion and exclusion criteria

We limited our search to peer-reviewed articles published in the last 10 years. We assessed article quality, study context and design, and outcomes. Inclusion criteria included original human studies that were on PubMed and Embase, written in English language, and those that specifically mentioned benign skin lesions treated with ablative lasers.

Exclusion criteria involved studies that were not accessible for full-text review, those without a discussion of treatment outcomes, adverse events or complications seen with ablative laser therapy, those that did not mention benign cutaneous lesions, and those that were not original clinical trials involving humans. Studies that did not specifically mention CO2 or Er:YAG lasers were also excluded.

A total of 136 records were generated using the above search terms, out of which a total number of 27 studies were shortlisted for our systematic review after screening the titles/abstracts and full texts for inclusion criteria.

Results

Study selections are detailed in Figure 1. 27 studies resulted after eliminating duplicates and following exclusion criteria.

Summary

This review compiles 27 studies consisting of 946 patients treated with either CO2 laser with or without an adjunct therapeutic modality (cohort 1) or Er:YAG with or without an adjunct therapeutic modality (cohort 2) for various dermatologic conditions.

Of the 27 studies included, 8 were randomized comparative studies, 10 were prospective split-face clinical trials, 5 were prospective cohort studies, and 4 were retrospective cohort studies. 26 of 27 studies discussed Fractional CO2 lasers and 4 of 27 studies discussed Er:YAG lasers. This literature review includes an aggregate of 946 patients. Regardless of treatment modality, the majority of adverse effects associated with the use of ablative laser treatments were transient. An analysis of the types of studies and their summative reported adverse effects are highlighted in Table 1. Erythema (n=319), pain (n=260), and hyperpigmentation (n=148) were the most commonly reported adverse effects in all studies and laser cohorts. Table 2 outlines the number of adverse events and percent of adverse events per laser cohort per study.

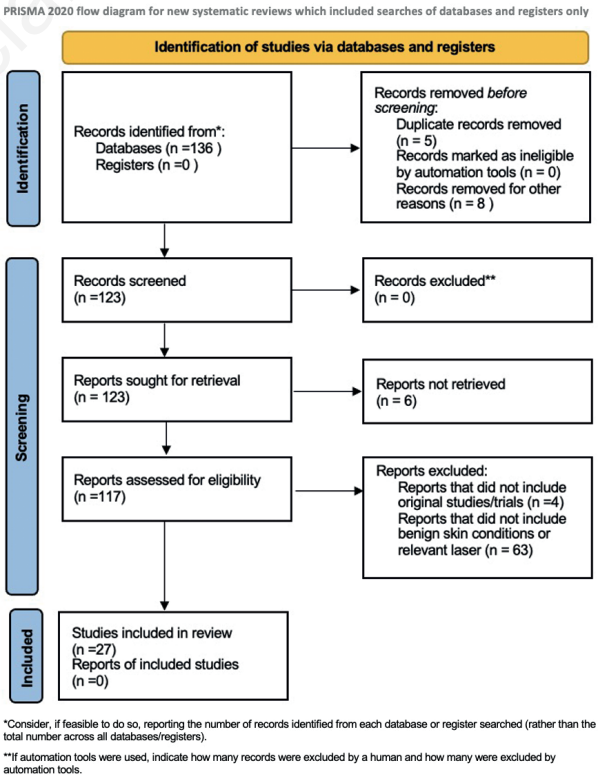

Figure 1. PRISMA 2020 Flowchart for selection of systematic review studies.

Table 1. Summative analysis of ablative lasers studies.

Author	Study type	Treatment	N (# of patients)	Laser Cohort 1	Laser Cohort 2	Summative adverse events of study
Osman *et al.*	Randomized comparative studies	Epidermal verrucous nevi	20	Fractional CO2 laser	Er:YAG laser	Erythema, hyperpigmentation, hypopigmentation, scarring, acneiform papules
Manuskiatti *et al.*	Randomized comparative studies	Atrophic acne scars	24	Fractional CO2 laser	Er:YAG laser	Pain, pinpoint bleeding, erythema, edema, crusting
Faghihi *et al.*	Randomized comparative studies	Atrophic acne scars	42	Fractional CO2 laser + punch elevation		Burning, erythema, crusting, pain, coagulum formation, pruritis
Feily *et al.*	Randomized comparative studies	Autologous hair transplants in refractory vitiligo	20	Fractional CO2 laser		Tenderness, erythema
Ahmed *et al.*	Randomized comparative studies	Ice-pick acne scars	28	Fractional CO2 laser		Pustules, hyperpigmentation
Zhang *et al.*	Randomized comparative studies	Atrophic acne scars	33	Fractional CO2 laser	Fractional microplasma radio frequency technology	Crusting, scaling, erythema, hyperpigmentation, pain
Tawfic *et al.*[1]	Randomized comparative studies	Post-acne hyperpigmentation	25	Fractional CO2 laser	Tranexamic acid	Burning pain, erythema
Sirithanabadeekul *et al.*[17]	Randomized comparative studies	Atrophic acne scars	25	Fractional CO2 laser	Fractional picosecond 1064-nm laser	Pain, burning, erythema, edema, hyperpigmentation
Galal *et al.*	Prospective split face clinical trial	Acne scars	30	Fractional CO2 laser	+ Platelet-rich plasma	Erythema, edema, crusting
Nilforoushzadeh *et al.*	Prospective split face clinical trial	Acne scars	30	Fractional CO2 laser	+ Subcision	Bruising, hyperpigmentation, erythema
Cameli *et al.*	Prospective split face clinical trial	Pho≤toaging and acne scars	10	Fractional CO2 laser	Fractional CO2 laser with radiofrequency	Burning, erythema, edema
Abdel Aal *et al.*	Prospective split face clinical trial	Acne scars	30	Combined autologous PRP plus ablative CO2 fractional laser	Ablative CO2 fractional laser	Erythema, acneiform eruption, hyperpigmentation
Vachiramon *et al.*	Prospective split face clinical trial	Solar lentigines	25	Fractional CO2 laser	Nd:YAG laser	Erythema, pain, PIH, hypopigmentation
Zhou *et al.*	Prospective split face clinical trial	Atrophic acne scars	22	Fractional CO2 laser + adipose-derived stem cell conditioned media		Edema, pain, crust
Hui Q *et al.*	Prospective split face clinical trial	Facial rejuvenation	13	Ultra-pulsed fractional CO2 laser + Platelet-rich plasma		Erythema, edema, crusting
Abdallah *et al.*	Prospective split face clinical trial	Acne scars	20	Fractional CO2 laser whole face	Fractional CO2 laser focal treatment	PIH, pain, peeling
Yang *et al.*	Prospective split face clinical trial	Atrophic acne scars	20	Fractional CO2 laser + pinprick	Super-pulse fractional CO2 laser "double layer mode"	Pain, edema, erythema, exudate, pinpoint bleeding, hyperpigmentation
Al Taweel *et al.*	Prospective cohort studies	Atrophic acne scars	40	Fractional CO2 laser + Platelet-rich plasma	Carboxytherapy + Platelet-rich plasma	Edema, pain, hyperpigmentation

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Table 1. Continued from previous page.

Author	Study type	Treatment	N (# of patients)	Laser Cohort 1	Laser Cohort 2	Summative adverse events of study
Helou *et al.* Fractional CO2 laser folliculitis, corneal abrasion	Prospective cohort Hyperpigmentation, studies	Acne scars and f acial rejuvenation				75
Elcin *et al.*	Prospective cohort studies	Atrophic acne scars	31	Fractional CO2 laser		Pain, erythema, edema, pinpoint bleeding, hyperpigmentation, acne exacerbation, hypertrichosis
Wang *et al.*	Prospective cohort studies	Acne scars	37	Fractional CO2 laser + IPL		Pain, pinpoint bleeding, exudate, erythema, edema, temporary desquamating micro crusts, comedones, PIH
Ochi *et al.*	Retrospective cohort studies	Acne scars	107	Fractional CO2 laser		Hyperpigmentation, blistering, crusting, aggravation of inflammatory acne, scarring
Tatlıparmak *et al.*	Retrospective cohort studies	Acne scars	72	Fractional CO2 laser + Fractional microneedle frequency		Pain, erythema, PIH, acne flare-up
Fang *et al.*	Retrospective cohort studies	Acne scars	82	Fractional CO2 laser		Erythema, PIH, hypopigmentation, acne flare, scars, pain
Maninder *et al.*	Retrospective cohort studies	Scars in the skin of color	42	Fractional CO2 laser		PIH, hypopigmentation, persistent erythema
Emam *et al.*	Prospective split face clinical trial	Atrophic acne scars	21	Microneedling radiofrequency	Fractional Er:YAG laser	Scaling, pain, erythema, burning, eczematization, hyperpigmentation
Lee *et al.*	Prospective cohort studies	Acne scars	22		Ablative non-fractional Er:YAG laser	Erythema, PIH, hypopigmentation, mild/moderate acne flare-up

Table 2. Adverse events experienced with ablative lasers.

Author	Laser Cohort 1	# Adverse events (Laser Cohort 1)	% Adverse events (Laser Cohort 1)	Laser Cohort 2	# Adverse events (Laser Cohort 2)	% Adverse events (Laser Cohort 2)	Erythema	Pain	PIH
Osman *et al.*	Fractional CO2 laser	Not reported	Not reported	Er:YAG laser	Not reported	Not reported			
Manuskiatti *et al.*	Fractional CO2 laser	Not reported	Not reported	Er:YAG laser	Not reported	Not reported			
Faghihi *et al.*	Fractional CO2 laser + punch elevation	42 (burning, erythema), 9 (PIH)	100% (burning, erythema), 21.4% (PIH)		N/A	N/A	x		x

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Table 2. Continued from previous page.

Author	Laser Cohort 1	# Adverse events (Laser Cohort 1)	% Adverse events (Laser Cohort 1)	Laser Cohort 2	# Adverse events (Laser Cohort 2)	% Adverse events (Laser Cohort 2)	Erythema	Pain	PIH
Feily *et al.*	Fractional CO2 laser	20 (tenderness, erythema)	100% (tenderness, erythema)		N/A	N/A	x		
Ahmed *et al.*	Fractional CO2 laser	2 (pustules), 2 (PIH)	7.1% (pustules), 7.1% (PIH)		N/A	N/A			x
Zhang *et al.*	Fractional CO2 laser	12 (PIH)	36.4% (PIH)	Fractional microplasma radio frequency technology	N/A	N/A			x
Tawfic *et al.*[1]	Fractional CO2 laser	25 (burning pain, erythema)	100% (burning pain, erythema)	Tranexamic acid	25 (burning pain, erythema)	100% (burning pain, erythema)	x	x	
Sirithanabadeekul *et al.*[17]	Fractional CO2 laser	25 (mild erythema, edema, crusting)	100% (mild erythema, edema, crusting)	Fractional picosecond 1064-nm laser	N/A	N/A	x		
Galal *et al.*	Fractional CO2 laser		Not reported	Not reported	+ Platelet-rich plasma	Not reported	Not reported		
Nilforoushzadeh *et al.*	Fractional CO2 laser	Not reported	Not reported	+ Subcision	Not reported	Not reported			
Cameli *et al.*	Fractional CO2 laser	Not reported	Not reported	Fractional CO2 laser with radiofrequency		Not reported	Not reported		
Emam *et al.*	Microneedling radiofrequency	17 (scaling), 3 (prolonged erythema, eczematization, PIH)	81% (scaling), 14.3% (prolonged erythema, eczematization, PIH)	Fractional Er:YAG laser	N/A	N/A	x		x
Abdel Aal *et al.*	Combined autologous PRP plus ablative CO2 fractional laser	4 (acneiform eruption)	13.3% (acneiform eruption)	Ablative CO2 fractional laser	2 (acneiform eruption)	6.67% (acneiform eruption)			
Vachiramon *et al.*	Fractional CO2 laser	9 (erythema)	36% (eryhthema)	Nd:YAG laser	8 (erythema)	32% (erythema)	x		
Zhou *et al.*	Fractional CO2 laser + adipose-derived stem cell conditioned media	Not reported	Not reported		Not reported	Not reported			
Hui Q *et al.*	Ultra-pulsed fractional CO2 laser + Platelet-rich plasma	13 (erythema, edema, crusting)	100% (erythema, edema, crusting)	N/A	N/A	x			
Abdallah *et al.*	Fractional CO2 laser whole face	2 (PIH)	10% (PIH)	Fractional CO2 laser focal treatment		3 (PIH)	15% (PIH)		x
Yang *et al.*	Fractional CO2 laser + pinprick	4 (persistent erythema), 3 (PIH)	20% (persistent erythema), 15% (PIH) layer mode"	Super-pulse fractional CO2 laser "double 2 (persistent erythema, PIH)	10% (persistent erythema, PIH)		x		x

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Table 2. Continued from previous page.

Author	Laser Cohort 1	# Adverse events (Laser Cohort 1)	% Adverse events (Laser Cohort 1)	Laser Cohort 2	# Adverse events (Laser Cohort 2)	% Adverse events (Laser Cohort 2)	Erythema	Pain	PIH
Al Taweel *et al.*	Fractional CO2 laser + Platelet-rich plasma	18 (edema), 14 (pain), 4 (PIH)	90% (edema), 70% (pain), 20% (PIH)	Carboxytherapy + Platelet-rich plasma	N/A	N/A		x	x
Helou *et al.*	Fractional CO2 laser	15 (PIH), 3 (folliculitis), 1 (corneal abrasion)	20% (hyperpigmentation), 4% (folliculitis), 1.3% (corneal abrasion)		N/A	N/A			x
Elcin *et al.*	Fractional CO2 laser	26 (erythema), 4 (edema), 17 (edema), 6 (PIH), 4 (acne), 5 (hypertrichosis)	83.9% (erythema), 12.9% (edema), 54.8% (edema), 19.4% (PIH), 12.9% (acne), 16.1% (hypertrichosis)		N/A	N/A	x		x
Lee *et al.*		22 (erythema), 10 (PIH), 1 (hypopigmentation), 5 (acne flare up)	100% (erythema), 45.5% (PIH), 4.5% (hypopigmentation), 22.7% (acne flare)	Ablative non-fractional Er:YAG laser	N/A	N/A	x		x
Wang *et al.*	Fractional CO2 laser + IPL	11 (comedones), 14 (PIH)	29.7% (comedones), 37.8% (PIH)		N/A	N/A			
Ochi *et al.*	Fractional CO2 laser	7 (PIH), 4 (blistering), 3 (crusting), 2 (aggravation of acne)	6.4% (PIH), 4% (blistering), 2.9% (crusting), 1.7% (aggravation of acne)		N/A	N/A			x
Tatlıparmak *et al.*	Fractional CO2 laser + Fractional microneedle frequency	52 (mild pain), 3 (erythema), 4 (PIH), 2 (acne flare-up)	72% (mild pain), 4.2% (erythema), 5.6% (PIH), 2.8% (acne flare)		N/A	N/A	x	x	x
Fang *et al.*	Fractional CO2 laser	82 (erythema, pain), 60 (PIH), 1 (hypopigmentation), 8 (acne flare-up), 2 (Post-treatment scar)	100% (erythema, pain), 73.2% (PIH), 1.22% (hypopigmentation), 9.8% (acne flare-up), 2.4% (Post-treatment scar)		N/A	N/A	x	x	x
Maninder *et al.*	Fractional CO2 laser	7 (PIH), 1 (hypopigmentation), 10 (persistent erythema)	16.6% (PIH), 2.4% (hypopigmentation), 24% (persistent erythema)		N/A	N/A	x		x

Both laser cohorts treated acne scars (n=801), scars in skin of color (n=42), post-acne hyperpigmentation (n=25), solar lentigines (n=25), facial rejuvenation (n=13), refractory vitiligo (n=20) and epidermal verrucous nevi (n=20). These studies include 8 randomized comparative studies, 10 prospective split-face clinical trials, 5 prospective cohort studies, and 4 retrospective cohort studies. Notably, only 1 out of 27 studies talked exclusively about scars in colored skin individuals. Erythema (n=319), pain (n=260), and hyperpigmentation (n=148) were the most commonly reported adverse effects in all studies and laser cohorts.

Atrophic acne scars

Randomized comparative studies

Manuskiatti *et al.* conducted a split-face comparative study on the efficacy and side effects of fractional CO2 *versus* Er:YAG lasers when treating atrophic acne scars (n=24).[8] Scarring improved significantly with both laser types from one month to six-month follow-up (p<.001), with no significant difference between the two types at one, three, and six month follow-up.[8] Pain scores on a scale of 1 to 10 were significantly higher on the CO2 laser side (5.8±2.0) compared to the Er:YAG side (3.2±1.4).[8] Side effects of pinpoint bleeding, erythema, edema, and crusting were comparable on both sides.[8]

Faghihi *et al.* studied the efficacy of punch elevation combined with fractional CO2 laser resurfacing in treating facial atrophic acne scarring.[9] In punch elevation, a punch biopsy tool is used to remove atrophic acne scar tissue from the skin. In all patients (n=42), transient post-treatment burning and erythema were noted.[9] Crusting, transient pain, coagulum formation, and pruritus were also noted.[9] Mild post-inflammatory hyperpigmentation (PIH) was noted in 21.4% of patients one month after the treatment, resolving within 6 months.[9] Hypopigmentation was not evident in any patients at the follow-up visits.[9]

Ahmed *et al.* studied the CO2 laser pinpoint irradiation technique *versus* the chemical reconstruction of skin scars technique (CROSS) in treating ice pick acne scars (n=28).[10] Pinpoint irradiation was applied to start at the forehead and proceed down to the rest of the face, while CROSS involved applying 100% trichloroacetic acid (TCA) on atrophic scars to induce inflammation and neo-collagenesis.[10] Of those treated with CO2 laser pinpoint irradiation, two patients developed pustules and two patients developed transient PIH.[10]

Zhang *et al.* compared the use of a fractional microplasma radio frequency technology and fractional CO2 laser for the treatment of atrophic acne scars (n=33).[11] The fractional CO2 laser side had a greater mean duration of post-therapy crusting and scaling (10.2±3.1 days) and erythema (12.3±6.8 days) than the fractional microplasma radiofrequency side (p<0.001).[11] Twelve patients receiving fractional CO2 laser treatment experienced PIH after 30 of 99 treatment sessions, with all cases graded mild, except for one, graded moderate.[11] The average duration of PIH was 45.8 days (range 14-90 days).[11] Mean visual analog scale (VAS) pain scores were greater with fractional microplasma radiofrequency treatments (5.9) compared to fractional CO2 treatment (4.3) (p=0.003).[11]

Sirithanabadeekul *et al.* conducted a split-face study on the treatment of atrophic acne scars with fractional picosecond 1064-nm laser *versus* fractional CO2 laser (n=25).[12] Average melanin concentration significantly increased at three months post-procedure in patients treated with CO2 laser (p=013).[12] Average fractional CO2 laser post-procedure pain was rated 3.4 and average post-procedure burning was 3.1.[12] All patients treated with fractional CO2 laser had mild erythema and edema that persisted in 84% of patients at the 1 week follow up and crusting. 24% of patients treated with CO2 laser developed PIH.[12]

Prospective split face clinical trials

Galal *et al.* compared the use of fractional CO2 laser *versus* combined platelet-rich plasma (PRP) and fractional CO2 laser in the treatment of acne scars (n=30).[13] The side with fractional CO2 laser and combined PRP had quicker resolution of erythema, edema, and crust formation (<3 days) than the side treated with fractional CO2 laser alone (5 to 7 days).[13]

Nilforoushzadeh *et al.* conducted a split-face study on the treatment of acne scars with fractional CO2 acne on the right side and fractional CO2 laser plus subcision on the left side of the face (n=30).[14] Subcision involves breaking down adhering acne scar tissue that is causing the scar to depress using a sharp needle.[14] On the combination therapy side, bruising was seen, lasting for one week (57%) and two weeks (43%).[14] PIH was also noted

on the combination therapy side. Erythema was noted in both therapies.[14]

Emam *et al.* conducted a split-face comparative study on the use of fractional Er:YAG laser *versus* micro-needling radiofrequency in the treatment of atrophic acne scars, using optical coherence tomography for assessment (n=21).[15] Side effects of scaling (81%), pain, erythema, and heat sensation were noted on the Er:YAG treated side.[15] Three patients experienced prolonged erythema, eczematization, and hyperpigmentation.[15]

Abdel Aal *et al.* compared combined autologous PRP plus ablative CO2 fractional laser *versus* only ablative CO2 fractional laser in the treatment of acne scars (n=30).[16] The right side of the face, which was PRP-treated, showed faster clearance of erythema following laser therapy than the left side, which was not PRP-treated (p=0.0052).[16] An acneiform eruption was noted at 13.3% on the PRP-treated side and 6.67% on the opposite side.[16] There was a significantly elevated incidence of PIH among darker skin phototypes (Fitzpatrick IV and V) as compared to lighter skin phototypes (Fitzpatrick I, II, III) (p=0.000).[16]

Zhou *et al.* studied fractional CO2 resurfacing for atrophic acne scars and skin rejuvenation in combination with adipose-derived stem cell conditioned media.[17] Edema, pain, and crust were noted, although "no hypertrophic or hypopigmented scarring" was observed.[17]

Abdallah *et al.* conducted a split-face study evaluating whole face area fractional CO2 laser (right side) *versus* focal acne scar treatment (FAST) fractional CO2 laser (left side) (n=20).[18] PIH was observed in 2 patients treated with whole face area fractional CO2 laser (10%) and 3 patients treated with FAST fractional CO2 laser (15%). Pain and peeling were also noted.[18]

Yang *et al.* conducted a split-face study of pinprick therapy combined with fractional CO2 laser on one side and super pulse fractional CO2 laser "double-layer" mode on the other side for the treatment of atrophic acne scars (n=20).[19] Pinprick therapy involves vertically piercing the base of the scar with a 1-mL syringe needle before pulsing with a fractional CO2 laser.[19] In the double-layer mode, a "first layer" involves local single-point high-energy irradiation (30 mj/cm^2).[19] Subsequently, the "second layer" involves low energy (10mj/cm2) treatment of all scar areas.[19] Immediately after either therapy, side effects such as pain, edema, erythema, exudate, and pinpoint bleeding, were noted.[19] For the super pulse fractional CO2 laser treatment side, 2 cases (10%) of persistent erythema with 2 to 3 days of regression and 2 cases (10%) of hyperpigmentation with 3-5 days of regression were noted.[19] For the combined treatment side, 4 cases (20%) of persistent erythema with 3-5 days of regression and 3 cases (15%) of hyperpigmentation with 10-15 days of regression were noted.[19]

Prospective cohort studies

Al Taweel *et al.* compared the efficacy of platelet-rich plasma (PRP) combined with fractional CO2 laser *versus* PRP combined with carboxytherapy for the treatment of atrophic acne scars (n=40).[20] The most common adverse effects noted in the PRP combined with the fractional CO2 laser group (n=20) included edema (90%), pain (70%), and hyperpigmentation (20%).[20]

Helou *et al.* studied the use of fractional CO2 laser for the treatment of acne scars and facial rejuvenation.[21] In 75 patients treated for facial rejuvenation or atrophic acne scars, hyperpigmentation (20%), folliculitis (4%), and corneal abrasion (1.3%) were noted.[21]

Elcin *et al.* conducted a prospective clinical study evaluating fractional CO2 laser for the treatment of facial atrophic acne scars (n=31).[22] Pain level VAS score was 5.32±2.62 (median 5, range 1–10).[22] Erythema was noted in 83.9% of patients on post-treatment day three and in 61.3% of patients on post-treatment day seven. Edema was noted in 12.9% of patients on post-treatment day three and in 3.2% of patients on post-treatment day seven.[22] Pinpoint bleeding was noted in 54.8% of patients on post-treatment day three and in 3.2% of patients on post-treatment day seven.[22] Hyperpigmentation lasting greater than one month duration which necessitated treatment was observed in 19.4% of participants.[22] 12.9% of participants had acne exacerbation and required treatment. Five female patients (16.1%) had hypertrichosis, which required epilation.[22] Overall, adverse effects in this study included but were not limited to pain, erythema, edema, pinpoint bleeding, hyperpigmentation, and hypertrichosis.

Lee SJ *et al.* studied the use of ablative non-fractional Er:YAG laser for atrophic facial acne scars.[23] In a study of 22 patients, erythema (100%), PIH (45.5%), hypopigmentation (4.5%), and mild-moderate acne flare-up (22.7%) were noted.[23]

Wang *et al.* evaluated acne scars and inflammatory acne treated with 4 to 6 Intense Pulsed Light (IPL) sessions and then 2 fractional CO2 laser sessions (n=37).[24]

All patients reported moderate pain for 3 to 12 hours after treatment.[24] All patients had pinpoint bleeding and slight exudation during treatment, erythema in the first seven days, which gradually faded over a month, edema in the first two days, which resolved within six days, and temporary desquamating microcrusts which resolved within 7 to 15 days.[24] 29.7% of patients developed comedones after treatment, which resolved after 1 to 2 weeks, and 37.8% developed PIH that resolved within 3 months.[24] No persistent PIH, blistering, erosions, scarring, or local infection were reported.[24]

Retrospective cohort studies

Ochi *et al.* conducted a retrospective study on the treatment of facial acne scars with a fractional CO2 laser (n=107).[25] Hyperpigmentation (6.4%), blistering (4%), crusting (2.9%), aggravation of inflammatory acne (1.7%), and scarring (0.6%) were noted. Hypopigmentation and bacterial or viral infection were not noted.[25]

Tatlıparmak *et al.* studied the use of combined fractional CO2 laser and fractional radiofrequency microneedling for the treatment of acne scars (n=72).[26] Temporary side effects, including mild pain (72%), erythema (4.2%), PIH (5.6%), and acne flare-up (2.8%), were noted.[26]

Fang *et al.* conducted a retrospective study on the treatment of acne scars with a fractional CO2 laser (n=82).[27] Erythema was noted in all patients (100%), which lasted >3 months in 16 patients (19.51%). PIH was noted in 60 patients (73.17%) and lasted >3 months in 26 patients (31.71%).[27] Additional side effects included hypopigmentation (1.22%), acne flare-up (9.76%), post-treatment scars (2.44%), and pain (100%).[27]

Epidermal verrucous nevi

Randomized comparative study

Osman *et al.* compared the efficacy of CO2 laser to Er:YAG laser in the treatment of epidermal verrucous nevi (n=20).[28] Both lasers showed equivalent outcomes with no significant differences in treatment response, patient satisfaction, duration of erythema, and side effects (hyperpigmentation, hypopigmentation, scarring, acneiform papules).[28] The only significant difference was the average time to re-epithelialization, which was 13.5 days with the CO2 laser and 7.9 days with Er:YAG laser ($p<0.0005$).[28] Osman *et al.* note that even though there was not a statistically significant difference between pigmentary changes (hyperpigmentation and hypopigmentation) between the two laser groups, there was a trend toward the CO2 laser having more pigmentary side effects and greater intensity of such changes.[28] Osman *et al.* discuss that this trend may be due to the Er:YAG lasers' higher ratio of "ablation to thermal damage in the dermis" than fractional CO2 laser.[28] This potentially decreases adjacent thermal diffusion and tissue damage.[28] Hyperpigmentation resolved for all patients with an unspecified topical bleaching cream.[28]

Autologous hair transplants in refractory vitiligo

Randomized comparative study

Feily et al studied the use of fractional CO2 laser pretreatment to autologous hair transplantations in refractory vitiligo (n=20).[29] All patients with fractional CO2 laser pretreatment experienced grade 1 tenderness and erythema, with tenderness resolving within 24 hours and erythema resolving within 2 weeks.[29]

Post-acne hyperpigmentation

Randomized comparative study

Tawfic *et al.* studied the use of tranexamic acid (TXA) *versus* fractional CO2 laser in post-acne hyperpigmentation.[30] All patients (n=25) experienced burning pain and mild erythema.[30] Burning pain was more with TXA intradermal injections.[30]

Photoaging and acne scars

Prospective split face clinical trial

Cameli *et al.* compared the treatment of photoaging and acne scars with CO2 laser alone to combined CO2 laser with radiofrequency.[31] Prolonged burning sensation was noted in the combination therapy side, however, this did not significantly affect the tolerability of treatment.[31] Post-treatment erythema and edema were reported as less visible on the combination therapy side.[31]

Solar lentigines

Prospective split face clinical trial

Vachiramon *et al.* reported that all patients (n=25) had pain immediately after both fractional CO2 and Nd:YAG laser treatment of solar lentigines.[32] Patients receiving treatment with Nd:YAG had significantly higher pain (4.01), as compared to those receiving treatment with fractional CO2 laser (2.04) (p<0.01). [32] Erythema was noted in 36% of patients treated with fractional CO2 laser and 32% of patients treated with Nd:YAG laser.[32] PIH was noted in 28% of patients receiving fractional CO2 laser treatment and 24% of patients receiving Nd:YAG treatment. [32] Two patients in each group developed hypopigmentation that eventually resolved.[32]

Facial rejuvenation

Prospective split face clinical trial

Hui Q *et al.* studied whether the combination of PRP and ultra-pulsed fractional CO2 laser had a synergistic effect on facial rejuvenation (n=13).[33] Erythema, edema, and crusting were the noted adverse effects in all patients (n=13). [33] The total duration of these adverse effects was significantly shorter in the combination group.[33]

Scars in skin of color

Retrospective cohort study

Maninder *et al.* investigated factors affecting outcomes of CO2 laser treatment of scars in the skin of color (n=42).[34] Adverse effects included PIH (16.6%), hypopigmentation (2.4%), and persistent erythema for 2 to 3 months (24%).[34]

Discussion

Summary

A notably higher rate of side effects was observed in CO2 laser therapies (n=610, 64.5%) when compared to Er:YAG and other laser cohorts (n=40, 4.2%). At least 2 studies did not report the number of side effects for both CO2 and Er:YAG laser therapies (Osman et al and Manuskiatti *et al.).* Only two studies directly compared the use of CO2 lasers to the use of Er:YAG lasers (Osman *et al.* and Manuskiatti *et al.*). The most common skin condition treated with both laser types as well as other adjunct modalities was acne scars.

Adverse events

Many side effects were commonly reported in these studies, regardless of the skin condition or type treated. The most common adverse events included erythema, pain, and hyperpigmentation with the use of CO2 laser and pain, hyperpigmentation, and scaling with the use of Er:YAG laser. Most of the side effects were transient and mild, however, there were a few concerning adverse events reported in various studies including blistering, folliculitis, corneal abrasion, hypertrichosis, and infection.[15,18,33] While these effects are important to note and monitor in patients, most are rare, treatable, and do not pose any long-term risk to the patients. In addition, an important adverse event of inflammatory acne flare-up was reported in several CO2 studies and one Er:YAG study, which may be distressing to patients who are being treated for acne scars.[5,15,16,18,19,32]

Recommendations

Both CO2 and Er:YAG lasers appear to have similar efficacy in the treatment of benign skin conditions.[1] The difference between these two lasers lies in the fact that Er:YAG may offer a benefit of fewer visible side effects such as erythema and hyperpigmentation, while CO2 may offer a benefit of less intraoperative and post-operative pain.[1,2] The choice of which laser to use should be discussed thoroughly between the patient and the physician to balance the efficacy and side effects with the unique needs of the patient.

Limitations

Limitations of our study include an unequal representation of CO2 lasers and Er:YAG lasers, which may make the direct comparison of adverse effects observed in both cases somewhat challenging. While some adverse

effects like erythema, pain, and hyperpigmentation were reported more frequently in most studies, other adverse effects and complications which may have existed in smaller numbers were not recorded. Additionally, several studies reported adverse events without defining the number of patients who experienced those events. This leads to uncertainty regarding how common a specific side effect may be in some studies. Moreover, there may be some deviation in reported adverse events seen with the use of both CO2 and Er:YAG lasers as some studies included complementary or adjunct treatments like platelet-rich plasma, tranexamic acid, fractional microplasma radio frequency technology, and chemical reconstruction of skin. Since different cutaneous conditions can be associated with certain specific adverse effects, the data from the studies we analyzed was not stratified to allow such distinctions to be made.

While this review offers a brief and most up-to-date overview of the most common adverse events and outcomes observed between Er:YAG and CO2 lasers in the treatment of various dermatologic conditions, concrete claims about the effectiveness of one laser over the other cannot be made due to the limited data comparing the two laser types parallel to each other. Moreover, there is an inadequacy of studies exploring the benefits of both laser types in treating other cutaneous conditions besides acne scars. Specifically, further research is warranted to more directly characterize the role of Er:YAG lasers in treating different skin conditions to aid clinical, pediatric, and cosmetic dermatologists to better treat their patients.

Conclusions

Ablative lasers such as CO2 and Er:YAG are generally used to treat numerous skin manifestations including acne scars, solar lentigos, pigmentary disorders, rhytids, skin laxity, and pore size due to their ability to target water and penetrate deeper layers of the skin. In this study, we conducted a comprehensive literature search to review and compare the nature of CO2 and Er:YAG laser therapies in current clinical practice. The data in this review demonstrates that CO2 and Er:YAG laser therapies provide patients with an efficacious means to treat common skin disorders with transient and limited side effects, including erythema (n=319), pain (n=260), and hyperpigmentation (n=148). Clinically, further communication regarding patient expectations and goals for the treatment of skin disorders should be explored by physicians to determine which specific laser therapy should be used. As newer laser modalities are introduced to the patient population, there is a need for expansion of clinical studies that can specifically compare and contrast one laser modality's efficacy and safety to another.

Contributions: HG, SK, FNM, BR, and ED had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: HG, KK. Acquisition, analysis, or interpretation of data: HG, SK. Drafting of manuscript: HG, SK, FNM, BR, ED, AP. Critical revision of the manuscript for important intellectual content: FNM, KK. Statistical Analysis: N/A. Obtained Funding: N/A. Administrative, technical, or material support: HG, FNM, KK. Study supervision: KK.

Conflict of interest: the authors declare no potential conflict of interest, and all authors confirm accuracy.

Ethics approval and consent to participate: not applicable.

Availability of data and materials: all data generated or analyzed during this study are included in this published article.

References

1. Ciocon DH, Doshi D, Goldberg DJ. Non-ablative lasers. Curr Probl Dermatol 2011;42:48-55.
2. Riggs K, Keller M, Humphreys TR. Ablative laser resurfacing: high-energy pulsed carbon dioxide and erbium:yttrium-aluminum-garnet. Clin Dermatol 2007;25:462-473.
3. Verma N, Yumeen S, Raggio BS. Ablative laser resurfacing. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022.
4. Zaresharifi S, Robati RM, Dadkhahfar S, *et al.* Efficacy and safety of cryotherapy, electrodesiccation, CO2 laser, and Er:YAG laser in the treatment of seborrheic keratosis. Dermatol Ther 2021;34:e15083.
5. Xu Y, Deng Y. Ablative fractional CO2 laser for facial atrophic acne scars. Facial Plast Surg 2018;34:205-219.
6. Raulin Ch, Grema H. Psoriasis vulgaris. Indikation fur den Laser? [Psoriasis vulgaris. An indication for lasers?]. Hautarzt 2003;54:242-247.
7. Lodhi A, Huzaira M, Khatri KA. Erbium:YAG laser skin resurfacing: a Pakistani experience. J Cosmet Laser Ther 2003;5:43-49.

8. Manuskiatti W, Iamphonrat T, Wanitphakdeedecha R, Eimpunth S. Comparison of fractional erbium-doped yttrium aluminum garnet and carbon dioxide lasers in resurfacing of atrophic acne scars in Asians. Dermatol Surg 2013;39:111-20.
9. Faghihi G, Nouraei S, Asilian A, *et al.* Efficacy of punch elevation combined with fractional carbon dioxide laser resurfacing in facial atrophic acne scarring: a randomized split-face clinical study. Indian J Dermatol 2015;60:473-8.
10. Ahmed R, Mohammed G, Ismail N, Elakhras A. Randomized clinical trial of CO2 laser pinpoint irradiation technique *versus* chemical reconstruction of skin scars (cross) in treating ice pick acne scars. J Cosmet Laser Ther 2014;16:8-13.
11. Zhang Z, Fei Y, Chen X, *et al.* Comparison of a fractional microplasma radio frequency technology and carbon dioxide fractional laser for the treatment of atrophic acne scars: a randomized split-face clinical study. Dermatol Surg 2013;39: 559-566.
12. Sirithanabadeekul P, Tantrapornpong P, Rattakul B, *et al.* Comparison of fractional picosecond 1064-nm laser and fractional carbon dioxide laser for treating atrophic acne scars: a randomized split-face trial. Dermatol Surg 2021;47:e58-e65.
13. Galal O, Tawfik AA, Abdalla N, Soliman M. Fractional CO2 laser *versus* combined platelet-rich plasma and fractional CO2 laser in treatment of acne scars: image analysis system evaluation. J Cosmet Dermatol 2019;18:1665-1671.
14. Nilforoushzadeh MA, Faghihi G, Jaffary F, *et al.* Fractional carbon dioxide laser and its combination with subcision in improving atrophic acne scars. Adv Biomed Res 2017;6:20.
15. Emam AAM, Nada HA, Atwa MA, Tawfik NZ. Split face comparative study of fractional ER:YAG laser *versus* microneedling radiofrequency in treatment of atrophic acne scars, using optical coherence tomography for assessment. J Cosmet Dermatol 2022;2:227-236.
16. Abdel Aal AM, Ibrahim IM, Sami NA, Abdel Kareem IM. Evaluation of autologous platelet-rich plasma plus ablative carbon dioxide fractional laser in the treatment of acne scars. J Cosmet Laser Ther 2018;20:106-113.
17. Zhou B-rong, Zhang T, Bin Jameel AA, *et al.* The efficacy of conditioned media of adiposederived stem cells combined with ablative carbon dioxide fractional resurfacing for atrophic acne scars and skin rejuvenation. J Cosmet Laser Ther 2016;18:138-148.
18. Abdallah MA, Gobrial CK, Gomah SG. Whole area *versus* focal acne scar treatment (FAST) of post acne-scars by fractional CO2 laser: a comparative study. QJM- Int J Med 2020;113 Suppl 1.
19. Yang Z, Jiang S, Zhang Y, *et al.* Self contrast study of pinprick therapy combined with super pulse fractional Co2 laser for the treatment of atrophic acne scars. J Cosmet Dermatol 2021;20:481-490.
20. Al Taweel AAI, Al Refae AAAS, Hamed AM, Kamal AM. Comparative study of the efficacy of platelet rich plasma combined with carboxytherapy vs its use with fractional carbon dioxide laser in atrophic acne scars. J Cosmet Dermatol 2019;18:150-155.
21. Helou J, Korkomaz J, Stephan F, Soutou B. Searching predictive factors of efficacy and safety in a fractional CO2 laser. Dermatol Ther 2020;33.
22. Elcin G, Yalici-Armagan B. Fractional carbon dioxide laser for the treatment of facial atrophic acne scars: prospective clinical trial with short and long-term evaluation. Laser Med Sci 2017;32:2047-2054.
23. Lee SJ, Kang JM, Chung WS, *et al.* Ablative non-fractional lasers for atrophic facial acne scars: a new modality of erbium:YAG laser resurfacing in Asians. Lasers Med Sci 2014;29:615-9.
24. Wang B, Wu Y, Luo YJ, *et al.* Combination of intense pulsed light and fractional CO(2) laser treatments for patients with acne with inflammatory and scarring lesions. Clin Exp Dermatol 2013;38:344-51.
25. Ochi H, Tan L, Tan WP, Goh CL. Treatment of facial acne scarring with fractional carbon dioxide laser in Asians, a retrospective analysis of efficacy and complications. Dermatol Surg 2017;43:1137-1143.
26. Tatlıparmak A, Aksoy B, Shishehgarkhaneh LR, *et al.* Use of combined fractional carbon dioxide laser and fractional microneedle radiofrequency for the treatment of acne scars: a retrospective analysis of 1 month treatment outcome on scar severity and patient satisfaction. J Cosmet Dermatol 2020;19:115-121.
27. Fang F, Yang H, Liu X, *et al.* Treatment of acne scars with fractional carbon dioxide laser in Asians: a retrospective study to search for predicting factors associated with efficacy. Laser Med Sci 2022;37:2623-2637.
28. Osman MAR, Kassab AN. Carbon dioxide laser *versus* erbium:YAG laser in treatment of epidermal verrucous nevus: a comparative randomized clinical study. J Dermatolog Treat 2017;28:452-457.
29. Feily A, Seifi V, Ramirez-Fort MK. Fractional CO2 laser pretreatment to autologous hair transplantation and phototherapy improves perifollicular repigmentation in refractory vitiligo: a randomized, prospective, half-lesion, comparative study. Dermatol Surg 2016;42:1082-8.
30. Tawfic SO, Abdel Hay R, Salim H, Elmasry MF. Tranexamic acid *versus* fractional carbon dioxide laser in post-acne hyperpigmentation. Dermatol Ther 2021;34:e15103.
31. Cameli N, Mariano M, Serio M, Ardigò M. Preliminary comparison of fractional laser with fractional laser plus radiofrequency for the treatment of acne scars and photoaging. Dermatol Surg 2014;40:553-61.
32. Vachiramon V, Panmanee W, Techapichetvanich T, Chanprapaph K. Comparison of Qswitched Nd: YAG laser and fractional carbon dioxide laser for the treatment of solar lentigines in Asians. Lasers Surg Med 2016;48:354-9.
33. Hui Q, Chang P, Guo B, *et al.* The clinical efficacy of autologous platelet-rich plasma combined with ultra-pulsed fractional CO2 laser therapy for facial rejuvenation. Rejuv Res 2017;20:25-31.
34. Maninder K, Richa R, Dinesh AP, Suman P. Factors affecting the outcome of fractional carbon dioxide laser resurfacing of various types of scars in skin of color. J Cosmet Dermatol 2021;21:3842-3847.