

REVIEW ARTICLE

Major clinical evidence of the optimization of the use of CO₂ fractional ablative laser with cells and molecules: a systematic review

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DOI: https://doi.org/10.54448/mdnt23301

Received: 05-15-2023; Revised: 07-09-2023; Accepted: 07-14-2023; Published: 07-23-2023; MedNEXT-id: e23301

Abstract

Introduction: Ablative fractional CO₂ laser skin resurfacing describes the process of removing the superficial epidermal and dermal layers of the skin to reduce the cutaneous signs of photoaging. The clinical efficacy and safety of exosomes, adipose tissue stem cells, platelet-rich plasma, and resveratrol as adjuvant therapy after ablative fractional CO₂ laser application are evidenced by the world literature. Objective: It was to carry out a systematic review to list the main clinical outcomes of the use of fractional ablative CO2 laser, with or without associated techniques, for facial aesthetic treatment. Methods: The systematic review rules of the PRISMA Platform were followed. The research was carried out from April to May 2023 in Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. Results and Conclusion: A total of 86 articles were found. A total of 32 articles were fully evaluated and 17 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 10 studies at high risk of bias and 37 studies that did not meet the GRADE. It was concluded that ablative fractional CO₂ laser offers a safe and effective treatment for disfiguring facial scars. It was shown that the improvement in the appearance and quality of the scar was significant for the patient, with a significant impact on the patient's quality of life. Based on these findings, we suggest including ablative fractional CO₂ laser in the concept of facial scar treatment. The results

demonstrate that the ablative fractional CO₂ laser of low fluence and low density is a safe and efficient option for the photorejuvenation of the face. Repeated application of ablative fractional CO₂ laser to skin with melasma can result in lasting improvement due to its destructive effect on melanocytes. Furthermore, the combined use of exosome gel with CO₂ laser resurfacing would provide synergistic effects on both the efficacy and safety of atrophic acne scarring treatments. ADSC-CM with CO₂ resurfacing is a good combination therapy for the treatment of atrophic acne scars and skin rejuvenation. The combined use of ablative fractional CO₂ laser and PRP obtained better results. Resveratrol can improve photoaging alone and add efficacy to fractional ablative laser treatment and decrease the adverse effects induced by fractional ablative laser.

Keywords: Facial aesthetics. Ablative fractional CO₂ laser. exosomes. Adipose mesenchymal stem cells. Platelet-rich plasma. Resveratrol.

Introduction

In the context of facial aesthetics, ablative fractional carbon dioxide (CO₂) laser skin resurfacing describes the process of removing the superficial epidermal and dermal layers of the skin to reduce the cutaneous signs of photoaging, as well as treating scars, actinic keratoses, seborrheic keratoses, and facial wrinkles. The use of lasers for ablation and resurfacing is based on the concept of selective thermolysis of the epidermal and dermal layers of the skin through the delivery of light energy. The skin's chromophores, melanin, and water absorb laser energy and emit



thermal energy, destroying the surrounding tissue [1].

In this regard, the implementation of pulsed CO_2 laser energy delivery and the subsequent development of the erbium-doped yttrium aluminum garnet (Er: YAG) laser further improved the accuracy and depth of skin ablation and reduced the incidence of adverse effects. A further refinement in skin resurfacing occurred in the early 2000s with the advent of fractional lasers, using microscopic and narrow light columns to treat a specific portion of the skin, enabling the reduction of adverse events and increasing the degree of therapeutic control [1,2].

In this context, the CO₂ laser remains an important system for aesthetic procedures. The lasers used in photo surgery have wavelengths that differ according to their intended use. With its mid-infrared wavelength of 10,600 nm, CO₂ laser energy is well absorbed in water. As the skin contains a very high percentage of water, this makes the CO₂ laser ideal for accurate and safe ablation with good hemostasis. In addition to its effectiveness in the ablation of benign raised lesions, the CO₂ laser has been reported to be effective in the field of aesthetics in the revision of acne scars, as well as in photorejuvenation [2].

With the addition of energy beam fractionation into myriads of microbeams, the fractional CO_2 laser offered a bridge between full ablative indications and nonablative skin rejuvenation systems. Technological advances in CO_2 laser construction have meant smaller spot sizes and greater precision for laser surgery and more flexibility in tip sizes and protocols for fractional CO_2 laser treatment [2-4].

Given the above, the present study aimed to carry out a systematic review to list the main clinical outcomes of the use of fractional ablative CO_2 laser, with or without associated techniques, for facial aesthetic treatment.

Methods

Study Design

The systematic review rules of the PRISMA Platform were followed. Available at: www.prisma-statement.org/. Accessed in: 05/22/2023.

Data Sources and Research Strategy

The search strategies for this systematic review were based on the keywords (MeSH Terms): "*Facial aesthetics. Ablative fractional CO₂ laser. Exosomes. Adipose mesenchymal stem cells. Platelet-rich plasma. Resveratrol*". The research was carried out from April to May 2023 in Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. In addition, a combination of keywords with the Booleans "OR", "AND" and the operator "NOT" were used to target scientific articles of interest.

Study Quality and Risk of Bias

Study quality was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument.

Results and Discussion Summary of Findings

A total of 86 articles were found. Initially, duplication of articles was excluded. After this process, the abstracts were evaluated and a new exclusion was performed, removing the articles that did not include the theme of this article, resulting in 42 articles. A total of 32 articles were evaluated in full and 17 were included and developed in this systematic review study (Figure 1). Considering the Cochrane tool for risk of bias, the overall assessment resulted in 10 studies with a high risk of bias and 37 studies that did not meet GRADE.



Source: Own authorship

Major Outcomes – Ablative Fractioned CO₂ Laser

One study gathered scientific information on the results of the use of fractional ablative CO₂, showing that 928 related articles were published in the last 18 years (2004-2021). The United States (US) dominates this field (312 documents), followed by Italy (289) and South Korea (88). Major research focuses include vulvovaginal atrophy, fractional photothermolysis, keloids, drug administration, gene expressions, facial acne scarring, resurfacing, vitiligo, and photodamage [5].

Lasers represent a relatively new group of devices used in surgical practice. Applications of lasers in medicine continue to advance with the addition of new



devices and the expansion of laser therapy indications. The process of targeting a specific chromophore is known as selective photothermolysis. The most common chromophores are water, tissue proteins, hemoglobin and pigment (eg melanin or tattoo pigment). Lasers that target water and interstitial proteins tend to vaporize tissue and are therefore termed ablative. In contrast, lasers that target hemoglobin and other pigments tend not to cause tissue destruction directly and are therefore known as nonablative. Therapeutic lasers are typically used for five different indications: vascular coagulation, pigment ablation, facial rejuvenation, tissue cutting or ablation, and hair removal. In general, complications of laser surgery can be mitigated by combining proper technique with proper patient and device selection [6].

In this regard, a prospective study performed a clinical and histological analysis of the effects on photorejuvenation after a single low-fluency, lowdensity fractional CO₂ laser treatment in 40 healthy women aged between 35 and 65 years. To histologically analyze the quantitative variation of type I and III collagen fibers, elastic fibers and epidermal thickness in D84, in addition to the clinical evaluation of the amount, length, thickness and depth of periocular wrinkles in the same period. A single fractional CO₂ laser session was performed on the face of the hole, using an 800 µm tip, 5% density and 10 mJ fluence with a single pass. The results of this study showed a significant clinical improvement in the amount, thickness, length and depth of periocular wrinkles. A significant increase in the amount of type III collagen fibers was observed at D84. Type I collagen fibers and elastic fibers did not have the same result, with a non-significant increase. The epidermal thickness tends to vary significantly [7].

Furthermore, a retrospective clinical study evaluated whether ablative treatment with fractional carbon dioxide laser (CO₂-AFL) can positively influence facial scarring and quality of life (QoL), with improved aesthetic appearance. Patients with facial scars who received treatment with CO₂-AFL (10,600 nm). Primary outcomes were changes in Patient and Observer Scar Scale (POSAS) and QoL (Short Form (SF-36). Sixteen patients with facial scars were included. Most scars were caused by burns (43.8%) or trauma (31.3%). emotional well-being and social functioning. In addition, the aesthetic result was significantly improved after treatment [8].

In addition, a study evaluated the ultrastructural effect of CO_2 fractional ablative laser (Fr CO_2) on facial melasma. A total of 11 patients with melasma were clinically evaluated by the Clinical Modified Area and Severity Index (MASI) score, treated by two fractional CO_2 laser sessions one month apart. Two 2 mm diameter punch biopsies were obtained from all

subjects, one before and the other 3 months after treatment. Clinically, significant improvement in pigmentation and 48% reduction in the (MASI) score were observed after two sessions of laser treatments. Microscopic analysis of the samples revealed a significant decrease in melanocyte count after treatment. Electron microscopic analysis of specimens after treatment revealed a significant decrease in the number and size of melanocytes and a significant decrease or complete absence of melanin granules in surrounding keratinocytes compared the to pretreatment specimens [9].

A retrospective study analyzed the efficacy and safety of fractional CO₂ laser for removal of dermal nevi A total of 330 patients with 684 facial nevi were observed. The fractional CO₂ laser was performed at 2month intervals until complete elimination. Global Assessment Scale (GAS) scores were used to assess overall results. A total of 554 nevi (81%) were successfully treated in one session. Eighty-nine (13%) and 34 (5%) required second and third sessions, respectively. Only seven (1%) required >3 sessions. At the end of one year, the patients' (87%) and physicians' (85%) GAS scores were classified as excellent and good, respectively. At one-year follow-up, fibrosis in 20 patients (3%), recurrences in 15 (2%), dimples in 12 (2%), scarring in 12 (2%), hyperpigmentation in 8 (1.5%) and hypopigmentation in 6 (1%) it was observed as a side effect [10].

Advanced Therapies and Associations with AFL- CO₂

A prospective, double-blind, randomized, split-face, 12-week study evaluated the clinical efficacy and safety of exosomes derived from adipose tissue stem cells as adjunctive therapy after the application of fractional CO2 laser for acne scars. A total of 25 patients received 3 consecutive sessions of full-face fractional CO2 laser treatment with follow-up evaluation. Post-laser treatment regimens were applied to each patient, one side of the face was treated with exosome gel derived from adipose tissue stem cells and the other side was treated with control gel. Sides treated with exosomes derived from adipose tissue stem cells achieved significantly greater improvement than control sides at the final follow-up visit. Treatment-related erythema was milder and posttreatment downtime was shorter in human adipose tissue applications on the side treated with stem cell-derived exosomes [11].

The use of an ablative pulsed CO_2 laser for skin rejuvenation is based on the gold standard status of the CO_2 modality and innovative post-treatment treatment, significantly reducing the complications of ablative treatment with pulsed CO_2 laser. Depending on the patient and the severity of the skin condition, each



treatment needs to be customized, which may also include fractional CO_2 lasers, fat grafting, facelifting, or any combination of these techniques [12].

Added to this, a study carried out by Zhou et al. (2016) evaluated the effects of adipose tissue-derived stem cell conditioned medium (ADSC-CM) on the efficacy and side effects after fractional carbon dioxide (R- CO₂) laser resurfacing in the treatment of individuals with scars. atrophic acne facials or in need of skin rejuvenation. A total of 22 subjects were included in the study and divided into two groups. Nine subjects were included in the skin rejuvenation group and thirteen subjects were included in the acne scars group, and all subjects underwent three sessions of R- CO₂. The ADSC-CM was applied to the R- CO₂ site on a randomly selected side of the face. Assessments were made at baseline, 1 week after the first treatment, and 1 month after each treatment. Outcome assessments included a subjective satisfaction scale; blind clinical evaluation; and the biophysical parameters of roughness, elasticity, skin hydration, transepidermal water loss (TEWL), and erythema and melanin index. ADSC-CM combined with R- CO2 increased satisfaction, skin elasticity, skin hydration, and decreased roughness and melanin index in acne scars and skin rejuvenation groups. Histological analysis showed that ADSC-CM increased dermal collagen density, and elastin density and arranged them in order [13].

Also, a randomized clinical trial was performed by Galal et al. (2019) to evaluate the effectiveness of CO₂ laser versus the combination of platelet-rich plasma (PRP) and fractional CO₂ laser in the treatment of acne scarring. A total of 30 patients with atrophic acne scarring lesions were included in this study. Patients were randomized to receive fractional CO₂ laser therapy on one side of the face, while the other side of the face was treated with fractional CO2 laser followed by intradermal injection of PRP. Follow-up using the skin analysis and photography camera system was done for three months. There was an improvement in the depth of the scar on both sides of the face. However, combined fractional CO₂ laser and PRP showed more significant improvement. Improvements in scar appearance and skin texture were reported by patients. No hyperpigmentation has been reported [14].

Still, another randomized clinical study elaborated by Abdel-Maguid et al. (2021) explored the impact of topical use of stem cell conditioned medium (SC-CM) after fractional carbon dioxide laser (FCL) versus combined FCL and platelet-rich plasma (PRP) or FCL alone in the treatment of atrophic scars from acne. A total of 33 Thirty-three patients were randomly assigned to two split-face groups. Group I (n = 17) received FCL plus topical SC-CM on one side or FCL plus saline on the other. Group II (n = 16) received FCL plus topical PRP or SC-CM. All patients had three monthly sessions. Clinical assessment was performed at each visit, with a final assessment after 3 months. No significant difference in clinical improvement of acne scars was observed between FCL/SC-CM and FCL sides only, while more significant and faster improvement was detected in FCL/PRP side compared to FCL/SC-CM side. Dermal collagen was increased and the type I procollagen gene was upregulated on both the FCL/PRP and FCL/SC-CM sides compared to the FCL-only sides [15].

Another randomized controlled clinical study developed by Kadry et al. (2018) evaluated the efficacy of PRP versus combined fractional CO₂ laser (Fr: CO₂) with PRP in the treatment of stable non-segmental vitiligo (NSV) lesions. A total of 30 patients with NSV were treated with PRP, Fr: CO₂ laser, and combined Fr: CO₂ laser with PRP. Intrapatient lesions were randomly divided into four groups. Each group was treated by a modality. The fourth group served as a control. Patients received six treatment sessions 2 weeks apart over 3 months and were followed up after 3 months. A significant reduction was demonstrated by analyzing vitiligo in the combined Fr: CO₂ laser with PRP and in the PRP-only groups than other groups. These results were confirmed by the mean improvement score per physician (MISP) and the VAS, with no statistical difference between them. The Fr: CO₂ laser combined with the PRP group showed minimal side effects. Regardless of the modalities, better improvement was observed in the trunk than in the face, extremities, and acral lesions with a significant reduction in all regions. On the face, the best result was with Fr: CO₂ laser with PRP. Trunk showed greater response with PRP. The upper limbs showed a greater response with the Fr: CO₂ laser combined with PRP. The lower limbs showed the greatest improvement with the Fr: CO₂ laser [16].

Finally, a randomized clinical trial conducted by Du et al. (2021) evaluated the efficacy and safety of resveratrol associated with the fractional CO₂ laser (AFL) ablative system in the treatment of cutaneous photoaging. A total of 32 subjects were assigned to the treatment group (TG) or control group (GC), respectively, and applied test product (resveratrol essence) or control product twice daily for 6 months. Each subject received an AFL treatment or no laser treatment on the left or right side of the face at random. All subjects in the TG had improvements in their signs of photoaging compared to pretreatment on both the laser and non-laser sides at 6 months. On the laser side, TG produced better improvement than GC at 6 months. On the laser side, the MI difference values in the TG at 2 months after enrollment (M2), M3, and M4 were more evident than those in the CG. On the side without laser,



the MI difference values in TG at M3, M4, M5, and M6 were more evident than those of the CG. TG subjects were more likely to have tingling and had a more rapid decrease in erythema, mild edema, and AFL-induced pigmentation compared to GC [17].

Conclusion

It was concluded that ablative fractional CO₂ laser offers a safe and effective treatment for disfiguring facial scars. It was shown that the improvement in the appearance and quality of the scar was significant for the patient, with a significant impact on the patient's quality of life. Based on these findings, we suggest including ablative fractional CO₂ laser in the concept of facial scar treatment. The results demonstrate that the low-fluency, low-density fractional CO₂ laser is a safe and efficient option for photorejuvenation of the face. Repeated application of fractional CO₂ laser to skin with melasma can result in lasting improvement due to its destructive effect on melanocytes. Furthermore, the combined use of exosome gel with CO₂ laser resurfacing would provide synergistic effects on both the efficacy and safety of atrophic acne scarring treatments. ADSC-CM with CO₂ resurfacing is a good combination therapy for the treatment of atrophic acne scars and skin rejuvenation. The combined use of fractional CO₂ laser and PRP obtained better results. Resveratrol can improve photoaging alone and add efficacy to fractional ablative laser treatment and decrease the adverse effects induced by fractional ablative laser.

Acknowledgement

Not applicable.

Funding

Not applicable.

Ethical Approval Not applicable.

Informed consent Not applicable.

Data sharing statement No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

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References

- Verma N, Yumeen S, Raggio BS. Ablative Laser Resurfacing. 2023 Apr 23. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 32491406.
- Omi T, Numano K. The Role of the CO2 Laser and Fractional CO2 Laser in Dermatology. Laser Ther. 2014 Mar 27;23(1):49-60. doi: 10.5978/islsm.14-RE-01.
- Ziai K, Wright HV. Carbon Dioxide Laser Rejuvenation of the Facial Skin. Clin Plast Surg. 2023 Jul;50(3):421-436. doi: 10.1016/j.cps.2022.12.007.
- Ziai K, Wright HV. Carbon Dioxide Laser Rejuvenation of the Facial Skin. Facial Plast Surg Clin North Am. 2022 Aug;30(3):331-346. doi: 10.1016/j.fsc.2022.03.007.
- Zou B, Zheng W, Pan H, Yang B, Liu Z. Research trends and hotspot analysis of fractional carbon dioxide laser: A bibliometric and visualized analysis via Citespace. J Cosmet Dermatol. 2022 Nov;21(11):5484-5499. doi: 10.1111/jocd.15267.
- Prohaska J, Hohman MH. Laser Complications. 2023 Mar 1. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 30335281.
- Jordão JM, Stoliar MFF, Melo SS, de Campos GLM, de Forville Mesquita LA, Skare TL. Lowfluence and low-density CO2 laser: histological analysis of collagen fiber changes in skin and its clinical repercussions in photorejuvenation. Lasers Med Sci. 2022 Mar;37(2):905-911. doi: 10.1007/s10103-021-03330-0.
- Meynköhn A, Fischer S, Neuss C, Willkomm LM, Kneser U, Kotsougiani-Fischer D. Fractional ablative carbon dioxide laser treatment of facial scars: Improvement of patients' quality of life, scar quality, and cosmesis. J Cosmet Dermatol. 2021 Jul;20(7):2132-2140. doi: 10.1111/jocd.13850.
- El-Sinbawy ZG, Abdelnabi NM, Sarhan NE, Elgarhy LH. Clinical & ultrastructural evaluation of the effect of fractional CO2 laser on facial melasma. Ultrastruct Pathol. 2019;43(4-5):135-144. doi: 10.1080/01913123.2019.1673861.
- **10.** Köse O. Efficacy of the carbon dioxide fractional laser in the treatment of compound and dermal



facial nevi using with dermatoscopic follow-up. J Dermatolog Treat. 2019 Aug;30(5):498-502. doi: 10.1080/09546634.2018.1529384.

- Kwon HH, Yang SH, Lee J, Park BC, Park KY, Jung JY, Bae Y, Park GH. Combination Treatment with Human Adipose Tissue Stem Cell-derived Exosomes and Fractional CO2 Laser for Acne Scars: A 12-week Prospective, Double-blind, Randomized, Split-face Study. Acta Derm Venereol. 2020 Nov 4;100(18):adv00310. doi: 10.2340/00015555-3666.
- Duplechain JK. Fractional CO2 resurfacing: has it replaced ablative resurfacing techniques? Facial Plast Surg Clin North Am. 2013 May;21(2):213-27. doi: 10.1016/j.fsc.2013.02.006.
- 13. Zhou BR, Zhang T, Bin Jameel AA, Xu Y, Xu Y, Guo SL, Wang Y, Permatasari F, Luo D. The efficacy of conditioned media of adipose-derived stem cells combined with ablative carbon dioxide fractional resurfacing for atrophic acne scars and skin rejuvenation. J Cosmet Laser Ther. 2016 Jun;18(3):138-48. doi: 10.2100/14764172.2015.1114628

10.3109/14764172.2015.1114638.

- 14. Galal O, Tawfik AA, Abdalla N, Soliman M. Fractional CO2 laser versus combined plateletrich plasma and fractional CO2 laser in treatment of acne scars: Image analysis system evaluation. J Cosmet Dermatol. 2019 Dec;18(6):1665-1671. doi: 10.1111/jocd.12909.
- Abdel-Maguid EM, Awad SM, Hassan YS, El-Mokhtar MA, El-Deek HE, Mekkawy MM. Efficacy of stem cell-conditioned medium *vs.* platelet-rich plasma as an adjuvant to ablative fractional CO₂ laser resurfacing for atrophic post-acne scars: a split-face clinical trial. J Dermatolog Treat. 2021 Mar;32(2):242-249. doi: 10.1080/09546634.2019.1630701

10.1080/09546634.2019.1630701.

- Kadry M, Tawfik A, Abdallah N, Badawi A, Shokeir H. Platelet-rich plasma versus combined fractional carbon dioxide laser with platelet-rich plasma in the treatment of vitiligo: a comparative study. Clin Cosmet Investig Dermatol. 2018 Nov 8;11:551-559. doi: 10.2147/CCID.S178817.
- Du YM, Zeng J, Li M, Wang YB, Wu Y, Qi RQ, Gao XH, Chen HD. Efficacy and safety of Resveratrol combined with Ablative Fractional CO₂ laser system in the treatment of skin photoaging. J Cosmet Dermatol. 2021 Dec;20(12):3880-3888. doi: 10.1111/jocd.14569.



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