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CASE SERIES

Fractional Carbon Dioxide Laser Combined with Secukinumab in the Treatment of Refractory Psoriasis Lesions on the Lower Legs

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Abstract: Psoriasis is a chronic autoimmune skin disorder characterized by high morbidity and a tendency for recurrence. Although biologic therapy for lesion clearance can achieve PASI 90/100, refractory sites remain challenging to completely clear, particularly on the lower legs and elbows. To explore the efficacy of novel treatments for these resistant sites, we present a clinical observation on the safety and effectiveness of fractional carbon dioxide (CO2) laser therapy combined with secukinumab for four patients with moderate-to-severe plaque psoriasis. After receiving at least 3 months of maintenance treatment with secukinumab 300 mg, these patients received fractional CO_2 laser therapy aimed at refractory sites on the lower legs. Treatments were administered every four weeks for a maximum course of 16 weeks. All four patients demonstrated improvement in the treatment of psoriasis lesions at refractory sites following the combined treatment approach. However, the degree of improvement differed among individuals. Leg Psoriasis Area and Severity Index (Leg-PASI) scores were reduced by 50% to 88%, while leg Physician's Global Assessment (PGA) scores showed a reduction of 50% to 75%. And no adverse effects were observed.

Keywords: fractional carbon dioxide laser, refractory sites, psoriasis, secukinumab, lower legs

Introduction

Psoriasis is an immune-mediated, chronic, relapsing inflammatory disease characterized by abnormal proliferation of keratinocytes, with a global prevalence ranging from 0.09% to 5.1%.[1,2] Among these patients, over 90% present with plaque psoriasis.[3] This disease not only impacts the skin's appearance but also significantly impairs their quality of life. Treatments for moderate-to-severe plaque psoriasis include topical therapies, oral traditional immunosuppressants (eg, methotrexate, cyclosporine, retinoids), biologics targeting (eg, TNF-α inhibitor, IL-17A inhibitors, IL-23 inhibitors), as well as small molecule targeted drugs.[4] Despite advances in these therapeutic approaches, certain sites—particularly the scalp, elbows, and lower legs—remain refractory to treatment, often persisting even after the use of biologics.[5,6] The lesions, especially the lower legs, are notably prone to recurrence and are difficult to resolve.[6] Various therapeutic strategies have been employed to address these refractory sites, including biologic switching, topical treatments, increased doses of methotrexate and acitretin, intralesional steroid injections, narrowband ultraviolet B (NB-UVB) therapy, 308 nm excimer laser, and aminolevulinic acid-photodynamic therapy (ALA-PDT).[7–9] While these approaches offer some efficacy, they differ in terms of safety, cost, and efficacy.[8]

Switching biologic therapies can be costly and may offer uncertain efficacy, while the use of oral medications can increase hepatic burden. Consequently, enhanced topical treatment have emerged as a viable alternative. However, local injection of corticosteroids carries the risk of skin atrophy. Fractional carbon dioxide (CO_2) laser assisted drug delivery

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has been employed in the treatment of various dermatology, including proliferative scarring, keloids, vitiligo, psoriasis, precancerous skin lesions, and certain neoplastic diseases.[10] Nevertheless, data on the efficacy of fractional CO_2 lasers specifically for treating refractory psoriasis lesions remain limited both domestically and internationally. In a preliminary study, Maria Beatrice et al[11] demonstrated that CO_2 lasers could achieve complete clearance of psoriasis plaques in various refractory sites. Another study reported that the combination of Er: YAG laser and etanercept (TNF-α inhibitor) significantly improved the Target Plaque Severity Score (TPSS), although it did not show a significant advantage compared to etanercept alone or Er: YAG laser alone.[12] The mechanism of fractional CO_2 laser therapy is primarily based on the principle of fractional photothermolysis, by splitting the CO_2 laser beam into numerous tiny beams, also known as microscopic treatment zones (MTZs). These beams selectively target specific areas of the skin, without damaging the surrounding skin. The localized damage stimulates the skin's natural repair process, promoting collagen and elastin production, resulting in skin regeneration and reconstruction. Secukinumab is a fully human anti-IL-17A monoclonal antibody that mitigates the inflammatory response by selectively inhibiting IL-17A—a pivotal cytokine in psoriasis pathogenesis.[13] IL-17A is markedly upregulated in psoriatic skin, promoting keratinocyte proliferation and inflammatory cell infiltration, which contribute to skin damage.[4] By neutralizing IL-17A, secukinumab reduces inflammation and alleviates skin symptoms. Combining secukinumab with fractional CO_2 laser enhances treatment efficacy; the fractional CO_2 laser creates controlled micro-injuries in the skin, minimally invasively stimulating skin regeneration and facilitating drug penetration. This combined approach accelerates inflammation resolution and skin barrier restoration, leading to faster and more effective improvement of psoriatic lesions. Therefore, this study aims to observe the clinical efficacy and safety of fractional CO_2 laser therapy combined with secukinumab in treating four cases of refractory psoriasis lesions on the lower legs.

Patients and Methods

This study was conducted at Guangzhou Dermatology Hospital from October 2022 to October 2023, involving four patients with chronic plaque psoriasis affecting more than 10% of their body surface area (BSA). Signed consent was obtained from each patient before enrollment. All participants had received at least three months of treatment with secukinumab 300 mg subcutaneous injection, leaving refractory lesions that persisted on the lower legs.[14] The study was conducted according to the Declaration of Helsinki principles and was approved by the Ethics Committee (gzsp202309). Pregnant, lactating women and children were excluded. Also, patients with concomitant renal, hepatic, and hematological abnormalities were excluded. To assess treatment efficacy, we collected the Physician's Global Assessment (PGA) and Leg Psoriasis Area and Severity Index (Leg-PASI), calculated on the Lund and Browder estimation method, at week 0, 4, 8, 12, and 16.[15] The PGA and Leg-PASI scores were independently assessed by two specialized dermatologists, with final results calculated as the mean of their evaluations.

Instrument

Fractional CO_2 laser (Model: CHX-100H, Wuhan Gaoke Hengda Optoelectronics Co., Ltd., rated optical power 20W, fractional scanning energy 10–250mJ/cm², maximum scanning area 15mm × 15mm).

Treatment Protocol

Following the initiation of biologic therapy, resistant lesions remained. Combined treatment with fractional CO2 laser was administered once every 4 weeks. The number of treatments was adjusted according to the patient's response, ranging from 1 to 4 times. The treatment parameters were set as follows: fractional mode, energy density of 60–100 mJ/cm², a spacing of 0.3 mm, and fractional coverage of 20%.

Preoperatively, the plaque was anesthetized with compound lidocaine cream. The handpiece was held perpendicular to the skin surface. Adjacent pulses were given and overlapping was avoided. The entire lesion area, along with 5 mm of surrounding skin, was evenly scanned. The endpoint of the treatment was indicated by the appearance of dense punctate crusting within the lesion, accompanied by punctate bleeding, oozing, or erythema of the surrounding skin. Following the laser treatment, ice packs were applied for half an hour. Meanwhile, secukinumab was administered as a 300 mg subcutaneous injection at the routine injection site.

Case Report

Patient 1

The patient is a 32-year-old Chinese male with a body mass index (BMI) of 34.2 and a 15-year history of psoriasis, complicated by diabetes and hypertension. Previous treatments, including methotrexate, topical corticosteroids, and calcipotriol betamethasone ointment, were ineffective. Psoriasis Area and Severity Index (PASI) and PGA scores were 42.5 and 4, respectively. After 16 months of monotherapy with secukinumab (300 mg), most of his psoriatic lesions had substantially cleared. However, thick, symmetrical, scaly plaques persisted on both lower legs, with a Leg-PASI score of 6.3 and a leg PGA score of 3. To further treatment, we initiated combined treatment with fractional CO_2 laser. Eight weeks after laser treatment, the Leg-PASI score decreased from 6.3 to 2.1, and the leg PGA score improved from 3 to 1. Both the Leg-PASI and leg PGA scores were reduced by 67%, with the residual plaques becoming noticeably flatter and showing minimal scaling.

Patient 2

The patient is a 32-year-old Chinese male with a BMI of 32.4 and a 16-year history of psoriasis. He has undergone various treatments, including methotrexate, cyclosporine, topical corticosteroids, and capotriol ointment, but his symptoms and rash have continued to recur. The PASI score was 38.5, PGA score was 4. After receiving monotherapy with secukinumab (300 mg) for 3 months, most of the psoriatic lesions on his body significantly cleared, leaving behind symmetrical, scaly, dark red plaques on the anterior aspects of both shins, with a Leg-PASI score of 16.8 and a leg PGA score of 4. The patient underwent a combined treatment approach using the fractional CO2 laser to further improve the residual lesions. After 16 weeks of laser treatment, the Leg-PASI score decreased from 16.8 to 2.1, and the leg PGA score improved from 4 to 2, representing reductions of 88% and 50%, respectively. The residual plaques became significantly flatter, with scaling nearly resolved and only mild pigmentation remaining.

Patient 3

The patient is a 32-year-old Chinese male with a BMI of 26.4 and a 5-year history of psoriasis. He has previously undergone treatment with methotrexate, acitretin, topical corticosteroids and phototherapy, with unsatisfactory results. PASI and PGA scores were 32.4 and 4, respectively. After 10 months of monotherapy with secukinumab (300 mg), most of the psoriasis lesions had significantly cleared, leaving behind symmetrical, scaly plaques of varying sizes on lower legs, with a Leg-PASI score of 19.4 and a leg PGA score of 4. After 16 weeks of fractional CO_2 laser treatment, Leg-PASI and leg PGA scores decreased to 7 and 2, respectively, both representing a 50% reduction. Additionally, the thickness of the plaques was noticeably reduced.

Patient 4

The patient is a 37-year-old Chinese male with a BMI of 24.2 and an 8-year history of psoriasis. He had previously undergone various treatment methods, including methotrexate, cyclosporine, acitretin, topical corticosteroids, calcipotriol ointment, and calcipotriol betamethasone ointment, but his symptoms and rashes continued to recur. The PASI score was 37.4, and the PGA score was 4. After 3 months of monotherapy with secukinumab (300 mg), most of his psoriasis lesions had cleared, with a scaly plaque remaining on the extensor side of the left lower leg. The Leg-PASI score was 1.225, and the PGA score for the left lower leg was 4. After 4 weeks of fractional CO_2 laser treatment, the Leg-PASI score decreased from 1.225 to 0.175, and the PGA score for the left lower leg decreased from 4 to 1. The Leg-PASI and leg PGA scores were reduced by 86% and 75%, respectively. The plaque on the left lower leg completely resolved, leaving only mild pigmentation in the area (see Tables 1 and 2, and Figures 1 and 2).

As of the date of manuscript submission, one patient had discontinued treatment for 6 months, while three patients continued on secukinumab, with no recurrence or worsening observed in any case.

Table 1 The Demographic and Clinical Characteristics of Psoriasis Patients

Variable	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	32	32	32	37
Sex	Male	Male	Male	Male
BMI	34.2	32.4	26.4	24.2
Other diseases	Diabetes; high blood pressure	No	No	No
Course of diseases (years)	15	16	5	8
Leg-PASI (pre-treatment)	6.3	16.8	14	1.225
Leg-PGA (pre-treatment)	3	4	4	4
Dosage of Secukinumab	300mg	300mg	300mg	300mg
Number of months of secukinumab injections prior to treatment	16	3	10	3

Table 2 Fractional CO2 Laser Treatment for Psoriasis Lesions on the Lower Legs

Patient	Site	Scale	Erythema	Thickness	Laser Frequency	Laser Energy	Adverse Effects	Results
1	Both legs	Severe	Severe	Moderate	2	60–60	No	Thin plaques, few scales
2	Both legs	Severe	Severe	Moderate	4	100–100-80-80	No	Thin plaques, few scales
3	Both legs	Severe	Moderate	Severe	4	100–100-90-90	No	Slightly thin plaques
4	Left leg	Moderate	Minimal	Minimal	1	60	No	Complete disappearance

Discussion

Recent studies have shown that psoriasis is a disease associated with immune dysregulation.[2] Its pathogenesis involves abnormal activation and infiltration of immune cells, particularly T lymphocytes.[16] These abnormal T lymphocytes infiltrate the skin, leading to an inflammatory response and rapid proliferation of epidermal cells, resulting in a host of abnormalities in the expression of cell surface molecules and cytokines takes place within the psoriatic epidermis.[16] This immune dysfunction may manifest differently across various body sites, particularly in areas prone to pressure, such as the lower extremities. A study by Hjuler et al[6] supports this view, finding that even after biologic treatment, the lower legs remain one of the most common refractory sites for psoriasis, with a prevalence ranging from 24.7% to 49.3%. The findings of our study further corroborate this, as residual lesions persisted on the lower legs in all four patients we observed, despite secukinumab treatment. Possible reasons for this include the greater pressure on the lower extremities and the larger diameter of capillary networks in the leg lesions, leading to delayed treatment response or sustained disease activity.[17]

Fractional CO_2 laser can improve skin microcirculation, and increase the supply of local immune cells and nutrients, thereby enhancing drug absorption and shortening lesion clearance time. However, the local injury may lead to new lesions or Koebner phenomenon by altering the local immune environment.[3,18] In 1982, Eyre and Krueger[19] reported that after removal of psoriatic plaques by a hand-held dermatome, 67% of them showed an "inverse Koebner" phenomenon. On the contrary, with the use of the same dermatome to remove uninvolved skin, psoriatic lesions were induced in 25%. Remarkably, our subjects did not experience the Koebner phenomenon. This could be attributed to secukinumab's effective inhibition of IL-17A, which significantly reduces skin inflammation and may further reduce the occurrence of the Koebner phenomenon. Additionally, laser by the use of a specific wavelength, we achieve the destruction of specific molecules (or chromophores), allowing better localization of thermal energy and minimization of damage to the surrounding tissue, unlike diffuse and uncontrolled skin damage, thereby preventing the occurrence of a Koebner phenomenon.[20] Moreover, Saiag et al[21] suggested that laser treatment penetrating the dermis might influence various types of fibroblasts or hyperproliferative keratinocytes through a bioregulatory effect, reducing the risk of the Koebner phenomenon in patients undergoing fractional CO_2 laser treatment.

In this study, all four patients with refractory lower leg lesions showed improvement with the combination of secukinumab and fractional CO_2 laser therapy; however, therapeutic efficacy varied. Previous research indicates that secukinumab responds well in the first year of treatment.[22] However, higher BMI in psoriasis patients may attenuate treatment efficacy due to the influence of adipose tissue on drug distribution and metabolism.[23] Notably, patient 4, who had a lower BMI than the other three patients, demonstrated significant therapeutic response as early as week 4 of combined treatment. This enhanced efficacy may be attributed

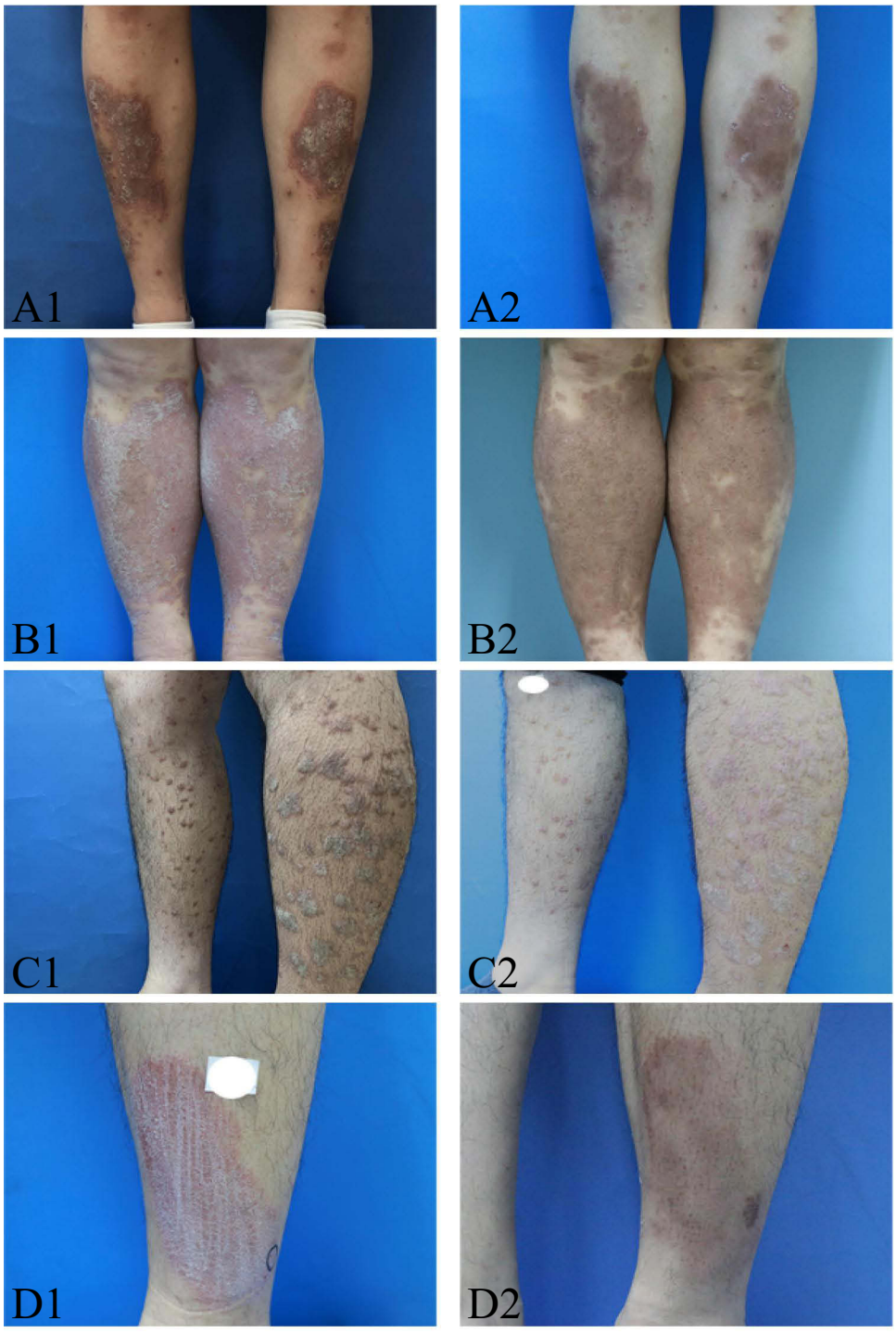

Figure 1 Clinical manifestations of four patients before and after fractional CO2 laser treatment. Patient 1 received 8 weeks of treatment before (**A1**) and after (**A2**); Patient 2 received 16 weeks of treatment before (**B1**) and after (**B2**); Patient 3 received 16 weeks of treatment before (**C1**) and after (**C2**); Patient 4 received 4 weeks of treatment before (**D1**) and after (**D2**).

to reduced subcutaneous fat in lower-BMI patients, allowing more direct laser penetration and action on localized lesions, thereby effectively mitigating the inflammatory response in the affected area. The third patient experienced slower lesion clearance, likely due to the thicker nature of the lesions, which may have required higher energy and more frequent laser treatments. No laser-induced complications, such as superficial burns, erythema, blister formation, hyperpigmentation, hypopigmentation, or pain, were observed in our study, indicating that secukinumab combined with fractional CO2 laser treatment has a favorable safety profile.

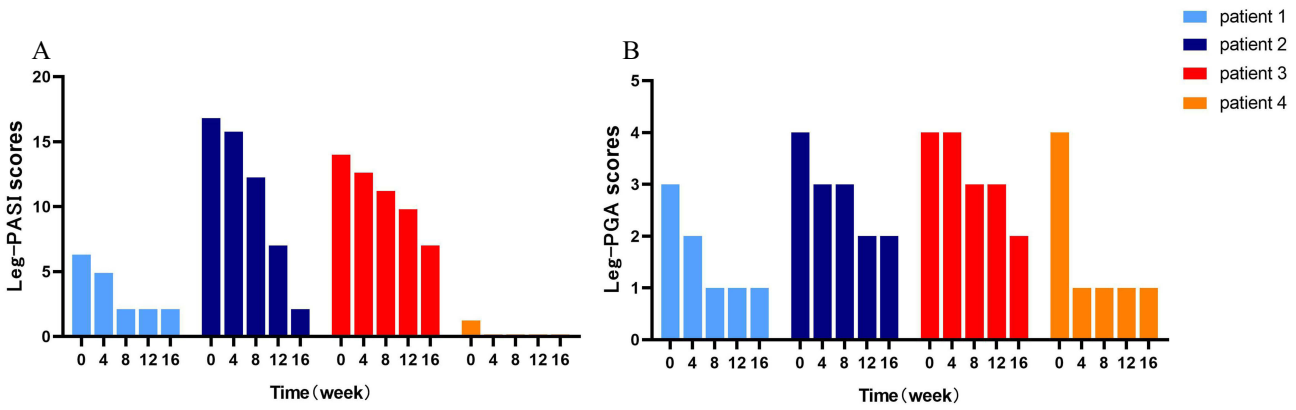

Figure 2 Leg-PASI scores (**A**) and leg PGA scores (**B**) of the four patients at weeks 0, 4, 8, 12, and 16.

The use of fractional CO2 laser therapy in combination with secukinumab can be an effective treatment for recalcitrant psoriatic lesions when secukinumab is not effective when alone. This combination therapy not only achieves a favorable balance between cost-effectiveness and therapeutic benefit but also demonstrates potential to enhance treatment success, patient satisfaction, and quality of life. As such, it offers a new treatment option for patients with psoriasis and may become an important complement to traditional treatments. However, our study has certain limitations, including small sample size, short follow-up period, different prior treatment regimens among patients, lack of a control group, lack of comparative analysis across different refractory sites, and insufficient analysis of the sequence of laser and biologic treatments or stratification based on the size of the treated area. These limitations affect the generalizability and reliability of our findings, as well as the precise evaluation of treatment efficacy.

Conclusion

Our findings showed that for refractory lower leg lesions post-biologic therapy, combined fractional CO_2 laser treatment can improve PASI response rates and reduce lesion recurrence. This offers a new strategy for the clinical management of refractory psoriatic lesions. Given the well-established long-term efficacy and safety profile of secukinumab, subsequent research should focus on assessing the long-term outcomes of combining secukinumab with fractional CO_2 laser therapy in real-world clinical settings, as well as exploring optimized treatment protocols to minimize the risk of therapeutic failure.

Data Sharing Statement

No datasets were generated or analyzed during the current study.

Consent for Publication

We have confirmed with the patients that the details of any images, videos, recordings, etc can be published, and patients informed consent for publication of their case details and images was obtained in written form. The Medical Ethics Committee of Guangzhou Dermatology Hospital has granted ethical approval for this study to publish case details (No. gzsp202309).

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Disclosure

The authors report no conflicts of interest in this work.

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