

CASE REPORT

Plaque-based sub-blistering dosimetry: Reaching PASI-75 after two treatments with 308-nm excimer laser in a generalized psoriasis patient

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Abstract

Background: Generalized UVB phototherapy has been established as an effective and safe treatment for chronic plaque-type psoriasis for decades and in recent years, targeted 308-nm excimer laser has emerged as an equally safe and more effective treatment option. While traditional dosimetry for laser has been determined either through minimal erythema dose (MED) or a combination of the patient's Fitzpatrick skin type and the level of plaque induration, we have developed "Plaque-based Sub-blistering Dosimetry" based on observations that administering anywhere from 8 to 16 multiples of MED to psoriatic plaques has resulted in clearance after one treatment with longer remission rates than the traditional dosing protocol. **Case report:** The authors describe a case in which a patient achieved PASI 75 following only two treatments with 308 nm excimer laser using this new protocol. Biopsies taken before and after treatment reveal a dramatic decrease in CD4+T cells as well as TNF-alpha- and IL-2-producing T cells.

Conclusion: This case demonstrates using a more aggressive dosing protocol determined by plaque testing is well-tolerated and can lead to excellent clearance with minimal side effects and comorbidity.

Keywords

Excimer, laser, plaque-based, psoriasis, sub-blistering

History

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Introduction

Generalized UVB phototherapy has long been used as an effective and safe treatment for chronic plaque-type psoriasis for decades and in recent years, targeted 308-nm excimer laser is emerging as an equally safe and more effective treatment option (1–3). The use of lasers has provided a way to administer phototherapy to lesional plaques only, avoiding light exposure of unaffected skin and allowing for higher doses of light per treatment. Because the laser is applied specifically to psoriatic skin, which is able to tolerate much higher doses of light, the clinician is able to dose more aggressively, resulting in faster clearing rates. Most laser protocols utilize the concept of "supra-erythemogenic phototherapy", in which optimized doses are significantly higher than the MED of non-psoriatic skin (2,4). Traditionally, dosimetry for this treatment has been determined either through minimal erythema dose (MED) or a combination of the patient's Fitzpatrick skin type and the degree of plaque induration. The dose is then increased incrementally at each treatment session, as tolerated, typically requiring 6 to 12 treatments to achieve PASI 75 (1).

Administering anywhere from 8 to 16 multiples of MED to psoriatic plaques has resulted in clearance at that location in as little as one treatment, as well as longer remission rates than when much lower doses are used (5–7). Based on these earlier observations, we proposed a new excimer laser dosing protocol called "Plaque-based Sub-blistering Dosimetry" in which the patient's psoriatic plaque, rather than uninvolved skin, is tested with incrementally increasing doses to determine the dose at which blistering is observed, and then treated just below that dose – at what we termed the "Plaque Sub-blistering Dose". This allows plaques to be treated at the most aggressive, yet tolerated, dose possible to achieve faster clearing. The authors describe a case in which a patient achieved PASI 75 after two treatments with 308 nm excimer laser using this novel "Plaque-based Sub-blistering Dosimetry".

Case description

A 42-year-old Hispanic man with Fitzpatrick skin type IV and a 10-year history of chronic plaque-type psoriasis was enrolled in a single site study investigating the use of excimer laser combined with topical therapy for the treatment of generalized psoriasis. The patient had failed traditional narrowband UVB "booth" phototherapy as well as topical agents. After a two-week washout, the patient was enrolled in the study with a baseline Psoriasis Area Severity Index (PASI) score of 11.5. During the screening visit, the patient's psoriatic plaque was tested with doses ranging from 300 to 1700 mJ/cm². The minimal blistering dose (MBD), or the first dose at which blistering was seen, was observed at 1500 mJ/cm², so a sub-blistering treatment dose of 1300 mJ/cm²

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Figure 1. (A) Patient photograph prior to treatment with 308-nm excimer laser. (B) Patient photograph after two treatments with 308-nm excimer laser treatment using the “Plaque-targeted Sub-blistering Dosimetry” plus clobetasol spray twice daily. (C) A close-up of the psoriatic plaque of the same patient prior to treatment. (D) A close-up of the same lesion after two treatments with the 308-nm excimer laser. Note the residual erythema is a result of laser treatment and not from psoriatic lesions.

was selected. To minimize phototoxicity, the patient applied clobetasol 0.05% ointment twice daily. One week after a single dose of excimer laser at 1300 mJ, the patient had significant clearing of his psoriasis. This dose was associated with some discomfort and blistering of the psoriatic plaques, which was noted as soon as ten hours after treatment. By day five, there was central healing of the skin and complete resolution of plaque induration, scaling and erythema in the treated areas and only post-inflammatory hyperpigmentation remained. During this time, the patient continued applying clobetasol spray twice daily as tolerated. Twelve days following the initial treatment the patient was assessed to have a PASI of 3.9 (PASI 66) and he was once again treated at a dose of 800 mJ. He was reassessed one week later to have a PASI score of 2.4, meaning he had a 79% improvement from baseline following two treatments of excimer laser (Figure 1).

In order to further investigate the mechanism of response to sub-blistering dose excimer laser therapy, pre- and post-treatment biopsy specimens were analyzed for functional differentiation of lymphocytes using flow cytometry (8). Results revealed a 10-fold reduction in cutaneous T cells when compared to pre-treatment lesional skin. T cell subset analysis revealed a

preferential reduction in the percentage of TNF- α -producing and IL-2-producing CD4+T cells in post-treatment lesional skin when compared to pre-treatment lesional skin (Figure 2). These cell types seemed to be selectively effected when compared to the more modest decrease in other cytokine-producing subsets, such as IL-17 secreting T cells.

Discussion

Based on prior studies that showed a superior response to treatment from aggressive therapy in localized area of plaques, we hypothesized that sub-blistering dose of excimer laser, selected by plaque-targeted testing, could result in superior results for generalized psoriasis. This 42-year-old patient reached PASI 79 after only two treatments with excimer laser and concurrent use of topical clobetasol spray twice daily. While both general and targeted UVB application increases apoptosis of T cells in the skin and decreases the amount of antigen presenting cells (9,10), it seems the administration of high doses of light may decrease the inflammatory response in the skin to a much greater extent, potentially leading to longer remission times (6). Certainly, the use of clobetasol spray may have contributed to the effectiveness

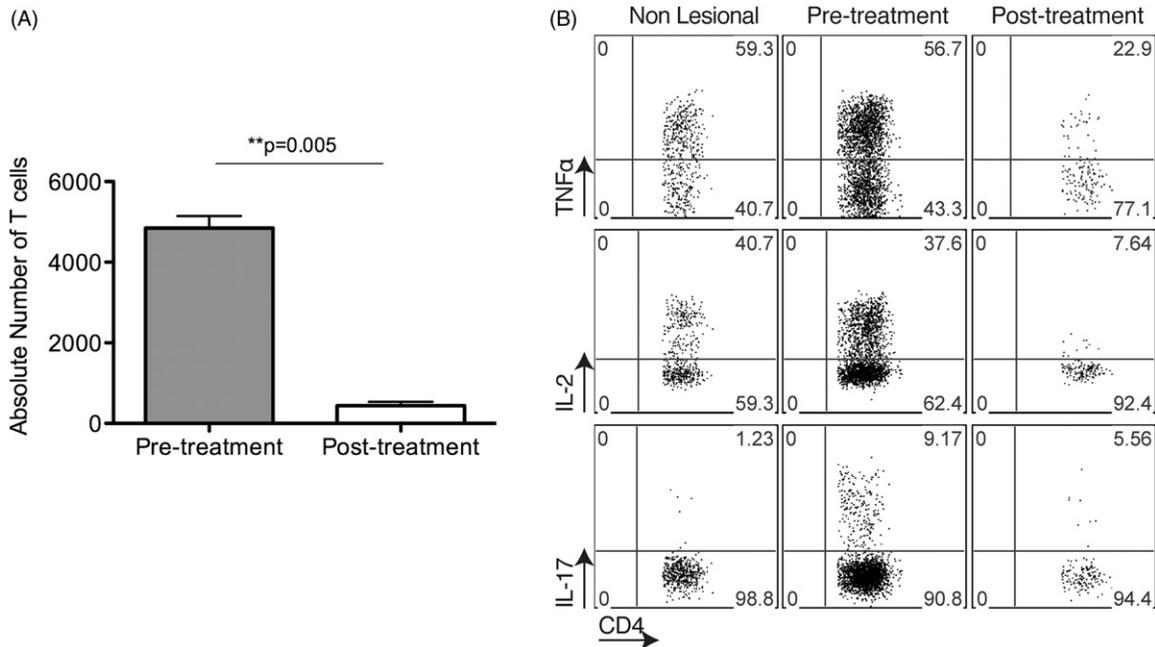


Figure 2. (A) Chart illustrating the significant reduction in absolute number of T cells in the skin biopsy prior to treatment and after treatment with high-dose excimer laser. (B) Flow cytometry analysis showing relative amounts of T-cells producing TNF- α , IL-2 and IL-17 in lesional skin before treatment, uninvolved skin without treatment and the area of a prior lesion after treatment with high-dose excimer laser.

of the high-dose excimer laser by not only enhancing the treatment of the psoriasis itself, but by possibly discouraging or decreasing any phototoxic reactions caused by the laser.

Our analysis of the pre-and post-treatment biopsies of a psoriatic lesion in this case revealed a significant change in the composition of immune cells in the skin. Overall, T cells were markedly reduced in excimer treated skin. Interestingly, T cells were reduced to levels lower than that seen in non-lesional skin taken from the same patient (Figure 2). This suggests that excimer laser therapy adversely affects the T cell niche in skin, as treatment with this modality reduces these cells to below baseline levels. This may explain the long duration of disease remission observed in patients treated with excimer laser. It is also of interest that not all T cells were reduced equally, as excimer laser therapy seemed to preferentially deplete TNF- α and IL-2 producers with little effect on IL-17 producing T cells (Figure 2). TNF- α concentrations are higher in psoriatic lesions than in unaffected skin of psoriatic patients and tend to decline with clearing of the lesions after effective therapy. This cytokine is produced by keratinocytes and leads to an increased expression of cellular adhesion molecules, which increase immune signals that are responsible for the pathogenesis of psoriasis. Similarly, IL-2 is expressed by a variety of immune cells and is required for their growth and survival. These results echo findings by Kagen et al., in which they showed a 5-fold increase in CD3+ T cell apoptosis in keratome biopsies just one hour following high-dose laser treatment as well as a 6-fold increase in caspase activity in intralesional T cells (6), a protease involved in the inflammatory response and has been implicated in keratinocyte differentiation. It appears that targeted high-dose excimer laser treatment increases apoptosis of specific pathogenic T cell subsets, leading to decreased expression of immune cells expressing inflammatory cytokines, resulting in rapid clearing of psoriatic lesions.

Conclusion

This is a case of a patient moderate-to-severe generalized psoriasis achieving PASI 75 in only two treatments using

“Plaque-based Sub-blistering Dosimetry”, a new, more aggressive laser dosing protocol that determines the highest dose the patient is able to tolerate. Because the primary downside of phototherapy as a treatment modality is the inconvenience and time-commitment of multiple treatments, this method of dosing may allow clinicians to treat psoriasis more effectively without the side effects of systemic medications. If this treatment can be further refined and made even more tolerable for a wider range of patients, this may lead to a much more effective and safe option that is usable for both localized and generalized psoriasis.

Declaration of interest

The authors received funding from Galderma and Photomedex. The authors alone are responsible for the content and writing of this paper.

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