

# New approach in the treatment of refractory vitiligo: CO<sub>2</sub> laser combined with betamethasone and salicylic acid solution

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## Abstract

The aim of this study is to evaluate the use of fractional carbon dioxide laser (CO<sub>2</sub>) with betamethasone and salicylic acid solution in the treatment of patients with refractory vitiligo in hands. Each hand of the patient was randomly assigned to one of two groups: lesion treated with fractional carbon dioxide laser associated with betamethasone and salicylic acid solution administration or lesion treated only with betamethasone and salicylic acid solution. We conclude that combined treatment with fractional carbon dioxide laser and betamethasone associated with salicylic acid solution could effectively and safely be used in the treatment of refractory vitiligo.

## KEYWORDS

CO<sub>2</sub> laser, salicylic acid, vitiligo

## 1 | INTRODUCTION

Vitiligo is the most prevalent pigmentary abnormality and occurs worldwide (Wolff et al., 2007). It presents an overall incidence rate between 0.1% and 2%, regardless of age, race, gender, ethnic origin, or skin color (Lotti, Gori, Zanieri, Colucci, & Moretti, 2008; Lotti et al., 2008; Parsad, Pandhi, Dogra, & Kumar, 2004; Wolff et al., 2007). It is an acquired abnormality that usually begins in childhood or early adulthood, with peak onset between 10 and 30 years old and is characterized by depigmented macules, well circumscribed stains that occur secondary to selective destruction of melanocytes (Kyriakis, Palamaras, Tsele, Michailides, & Terzoudi, 2009; Wolff et al., 2007).

Vitiligo seems to be transmitted by a multifactorial etiology and polygenic inheritance. The current pathogenesis has been attributed to autoimmune causes, oxidative stress, and/or sympathetic neurogenic disorder (Taieb & Picardo, 2009).

The treatment is based on the use of corticosteroids (CSs), calcineurin inhibitors, calcipotriol, ultraviolet light, UVA and NB-UVB (Felsen, Alikhan, & Petronic-Rosic, 2011). Laser therapy for vitiligo is a treatment that has gained popularity in the last decade. The laser operates by removing affected keratinocytes, increasing the penetration of substances such as CSs, among others (Bayoumi et al., 2012; Li et al., 2015; Wassef, Lombardi, Khokher, & Rao, 2013). However, the mechanism involved in enhancing the effectiveness of the combination of betamethasone solution and salicylic acid (SA) is still unknown.

## 2 | MATERIALS AND METHODS

This study was approved by the Ethics Research Committee of Jundiaí Medical School and all patients received information about the study and the procedure that would be performed. The Term of Informed Consent (IC) was signed.

Four patients, with stable vitiligo for at least six months, without topical and systemic treatment for three months, were included. Initially, the vitiligo type was determined, as well as duration and activity of the disease and the patient's phototype, by Fitzpatrick rating. Each patient was randomly assigned to the treatment with fractional laser carbon dioxide (CO<sub>2</sub>) associated with betamethasone solution and SA or only with betamethasone solution and SA.

Five fractional laser carbon dioxide sessions were made, with an interval of four weeks between them. During the session, cold air (20°C) was used to protect the skin and decrease the pain. The carbon dioxide (CO<sub>2</sub>) fractional laser (PIXEL CO<sub>2</sub>—Alma lasers) was used with a wavelength of 10,600 nm, fluence of 100 J/cm<sup>2</sup> with pulse duration shorter than 1 millisecond, pulse width of 500–1,000 microns, and pulse frequency of 25–500 Hz with the Roller-tip System Technology. The solution of betamethasone (0.05%) and SA (2.0%; Mantecorp Chemical and Pharmaceutical Industry—Brazil) was administered by the patient itself once a day, at night, every day. Patients were contacted every 15 days by telephone to assess the follow-up treatment and eventual doubts. The photographic record before and after the treatment was made with the same camera (Nikon D90 AF-S 105mm micro nikkor 1Ç2.8G).

TABLE 1 Information related to participants and patient satisfaction regarding the procedure

Patient	Age	Duration of the disease (years)	Previous treatment	Skin phototype	Level of satisfaction	Pain during the procedure	Adverse effects
I	21	15	yes	IV	Satisfied	2.5	Itchy skin
II	35	1	yes	V	Satisfied	1	absent
III	47	5	yes	III	Satisfied	2	absent
IV	26	13	yes	IV	Satisfied	1	absent

The objective analysis of the repigmentation percentage was made in photographs by two dermatologists collaborators. The blind study was rated excellent (repigmentation >75%); Good (50–75%); Moderate (25–50%), and minimum (<25%). The subjective analysis was done by completing an evaluation form on the degree of patient satisfaction in: very satisfied, satisfied, or dissatisfied. The patient also evaluated the pain of the procedure, on a scale of 0 to 10 in accordance with preliminary clinical character of pain, and adverse effects of the treatment.

### 3 | RESULTS

The study included the participation of four patients with vitiligo with symmetrical lesions in the hands, who attended the outpatient clinic of Jundiá Medical School in Sao Paulo, Brazil. The average age of all participants was 32.25 years old. The average time of onset disease among patients was 8.5 years. Among all patients, vitiligo that occurred on the hands was considered as a difficult treatment area and resistant to most treatments. All patients were satisfied with the results. In the propaedeutic pain scale between 0 and 10, it ranged from 1 to 2.5. Only 1 patient had itchy skin as an adverse effect. Infection, scarring, vitiligo worsening or Koebner phenomenon were not observed (Table 1).

After the sessions, the hands submitted to the carbon dioxide laser, betamethasone solution, and SA showed an excellent repigmentation rate (greater than 75%, Figure 1) in one patient; moderate (25–50%, Figure 2) in one patient; and minimal (less than 25%) in two patients. All patients of laser had some repigmentation rate, which did not happen with the control hand—betamethasone solution and SA isolated. For statistical analysis, the Wilcoxon test was used, resulting  $P = .12$ ; it was not considered statistically significant.

### 4 | DISCUSSION

The fractional ablative CO<sub>2</sub> laser is a new therapeutic concept that creates microscopic vertical canaliculi in the ablated tissue. It does not promote ablation of the whole epidermis, leaving intact skin tissue between necrotic coagulated columns. The penetration and distribution of topically applied drugs is then facilitated, since the canaliculi caused by the laser ablation extend into the dermis (Manstein, Herron, Sink, Tanner, & Anderson, 2004). In the present study, the laser was initially solitary performed, with subsequent association of betamethasone lotion and SA, taking advantage of the better penetration of the canaliculi provided by the laser, since the major limiting step for percutaneous absorption is the passageway through the stratum corneum.



FIGURE 1 Left: Before the treatment. Right: After five sessions of fractional carbon dioxide laser associated with betamethasone and salicylic acid solution administration. Patient with excellent repigmentation rate (greater than 75%)



**FIGURE 2** Left: Before treatment. Right: After five sessions of fractional carbon dioxide laser associated with betamethasone and salicylic acid solution administration. Patient with moderate repigmentation rate (25–50%)

Cohesion of epidermal cells in the skin depends upon desmosomes, which contain many proteins, including desmogleins. It has been found that SA, being an organic acid, extracts these proteins. As a result, the adhesion of corneocytes is decreased and the cohesion of epidermal cells is lost (Arif, 2015). Therefore, betamethasone might have increased its action. Furthermore, Jian et al. (2016) suggested that SA protects human melanocytes against  $H_2O_2$ -induced oxidative stress via Nrf2-driven transcriptional activation of HO-1.

Shin, Lee, Hann, and Oh (2012) investigated the effects of fractionated  $CO_2$  laser followed by the NB-UVB phototherapy in non-segmental vitiligo, suggesting that this combination may be effective and safe, achieving good results. Mohamed, Mohammed, Gomaa, and Eyada (2015) have studied the use of  $CO_2$  laser followed by 5FU in patients with acral vitiligo, resistant to treatment. The combination was considered a safe and tolerable technique.

As described above, several combinations of treatments using laser have been made, all showing good response (Bayoumi et al., 2012; Mohamed et al., 2015; Shin et al., 2012; Wassef et al., 2013). However, this is the first study that evaluates the effectiveness of carbon dioxide fractional laser ( $CO_2$ ) in combination with a solution of betamethasone and salicylic acid and we have a good result. One patient achieved a repigmentation rate between 75 and 100%, suggesting that this combination may be safe and effective in the treatment of refractory vitiligo in hands and could be effective in others areas of the body.

## 5 | CONCLUSION

The use of fractional carbon dioxide laser combined with betamethasone and SA solution could be a new therapeutic approach for the treatment of patients with refractory vitiligo. Further studies with a larger number of patients are required to define the protocol.

## CONFLICT OF INTEREST

No conflict of interest

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