

## Improvement of Microstomia in Scleroderma after Carbon Dioxide Laser Treatment

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### Key Words

Systemic sclerosis · Microstomia · Limited mouth opening · Carbon dioxide laser · Interincisal distance · Mouth Handicap in Systemic Sclerosis scale

### Abstract

Limited mouth opening (LMO) is a frequent complication of systemic sclerosis (SS). Its management is complex and there are limited treatment options. We report four patients with SS and severe LMO [interincisal distance (IID) <30 mm] treated with pulsed carbon dioxide (CO<sub>2</sub>) laser. Pulsed CO<sub>2</sub> laser treatment of the white lips was performed after all patients had signed a written informed consent in the absence of alternative treatment. Treatment was carried out under locoregional anaesthesia using a Sharplan 30C CO<sub>2</sub> laser in the Silk Touch<sup>®</sup> resurfacing mode. One to three laser sessions were performed at intervals of 8–12 months between sessions. Assessments were performed at 3 and 12 months with measurement of the IID using a ruler, calculation of the Mouth Handicap in Systemic Sclerosis (MHSS) scale and global evaluation by the patients. Adverse events were also reported. In all four patients, an improvement in IID occurred 3 months after the first session with a mean gain of +5 mm (range: 2–7). At 12 months, a mean gain of +8.5 mm (range: 7–10) in IID was observed. The MHSS score decreased by a mean of –14 (range: 11–17). All patients showed improvement of lip flexibility or mouth opening, allowing better phonation and mastication and easier dental care. Adverse effects were transient erythema and/or dyschromia. CO<sub>2</sub> laser appears to be effective and well tolerated in the improvement of LMO in SS.

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## Introduction

Systemic sclerosis (SS) is associated with functional consequences that significantly impact on patients' quality of life [1]. Progressive facial dermal fibrosis is responsible for limited mouth opening (LMO), which interferes with mastication and phonation. Basic oral hygiene care can become impossible [2]. Severe LMO is defined by an interincisal distance (IID) <30 mm [3]. The management of LMO is complex and there are limited treatment options available. We report four patients with SS associated with severe LMO who were treated with pulsed carbon dioxide (CO<sub>2</sub>) laser.

## Materials and Methods

### *Patients*

Between January 2012 and November 2014, four SS patients with severe LMO refractory to conventional physical therapy received pulsed CO<sub>2</sub> laser treatment of the white lips. The laser treatment was performed by C.B.L. All patients signed a written informed consent. This treatment is substantiated by the publication of Apfelberg et al. [4], who recommended CO<sub>2</sub> laser treatment of perioral rhytids in SS, and is effective in improving skin appearance without severe complications.

### *CO<sub>2</sub> Laser Procedure*

Prophylaxis of infectious complications associated with CO<sub>2</sub> laser was performed by the application of topical 2% sodium fusidate ointment (Fucidin®) twice a day into the nostrils, starting 5 days before the procedure and continuing until complete healing, and oral administration of valacyclovir (Zelitrex®) 500 mg daily, starting 2 days before the procedure and continuing until complete healing [5, 6].

CO<sub>2</sub> laser treatment was carried out under locoregional anaesthesia using 1% lidocaine solution containing 0.005 mg/ml adrenaline (Xylocaine adrenaline® 1%). Anaesthesia of the lips was obtained by infiltrating the infraorbital and mental nerves. If required, lidocaine solution was additionally infiltrated directly into the lip tissue. Saline-soaked gauze was placed in the mouth between the teeth and lips to prevent accidental teeth burns. The Sharplan 30C CO<sub>2</sub> laser (Sharplan Lasers, Lumenis SARL, Suresnes, France) used the Silk Touch® resurfacing mode with a 125-mm handpiece, 5 mm spot, 7 W, 0.39 ms. We performed 2–3 passes until contraction of the dermis was obtained. Each pass was carried out without overlapping the spots on the white lips, maintaining a distance of 2 mm from the commissures and the red lips. We did not remove the epidermis between each pass so as to prevent heat diffusion and reduce the risk of scarring (fig. 1) [7]. At the end of the treatment, equal quantities of 2% sodium fusidate ointment and sterile Vaseline® were applied three times daily to the white lips without dressing [6]. Paracetamol 1 g three times a day was used on an as-needed basis for pain. All patients were instructed to clean the treated white lips with sterile physiological saline solution and to continue application of sodium fusidate ointment and sterile Vaseline® mixture three times daily until complete healing (on average 12 days) to help healing and reduce the risk of infection [6]. The numbers of sessions (1–3) and the interval between two sessions (8–12 months) varied according to the patient's and physician's perception of clinical effectiveness.

### *Clinical Evaluation of Treatment*

Patients were evaluated 3 and 12 months after each session by I.B. or C.P. Physician assessment was based on measurements of IID at each visit. The measurement of IID was standardised. Maximum IID was measured using a small ruler, as the distance in mm between the upper and lower incisal edges of the right central incisors. The participants were requested to open their mouth as wide as possible [8]. Patient assessment was based on the Mouth Handicap in Systemic Sclerosis (MHISS) scale (0–48) [9], and a global clinical assessment using a three-point ordinal scale (+1 = improvement; 0 = no change; –1 = worsening) and to evaluate the response to the question: ‘What is improved by this treatment?’ In addition, pre- and posttreatment photographs were performed. Adverse events were reported at each visit.

## **Results**

### *Patient Characteristics*

Four nonsmoking female SS patients received laser treatment. The phototype varied from II to IV and the mean age was 52 years (range: 43–63). Two patients were diagnosed with diffuse SS with antitopoisomerase antibodies; one had scleromyositis with anti-PM/SCL antibodies and the other had CREST (calcinosis, Raynaud phenomenon, esophageal involvement, sclerodactyly and telangiectases) syndrome with anticentromere antibodies. Skin sclerosis had been present for at least 5 years in all patients. The mean modified Rodnan skin score was 15.5/51 (range: 12–18) and remained stable during the follow-up period. No patient received immunosuppressive therapy during or in the 12 months prior to laser treatment. No patient underwent physical therapy or practised stretching exercises to improve mouth opening during the follow-up period or in the 12 months prior to treatment. The initial mean IID and MHISS scores were 24.25 mm (range: 17–30) and 39 (range: 31–44), respectively.

### *Clinical Evaluation of Treatment*

In all patients, an improvement in IID was observed 3 months following the first CO<sub>2</sub> laser session with a mean gain of +5 mm (range: 2–7). In patients receiving a second laser session (n = 3), an additional mean gain of +1.66 mm (range: 1–3) in IID was observed 3 months after the second session. At 12 months, the mean gain in IID was +8.5 mm (range: 7–10), corresponding to an improvement in IID of about 37.37% (range: 24.1–58.8) (fig. 2, fig. 3). The MHISS score was evaluated in three patients and improved by a mean of –14 (range: 11–17). All patients assessed the response to therapy as +1 = improvement. All patients showed an improvement in lip flexibility and/or mouth opening with better phonation and mastication and/or easier dental care. Demographic, clinical and therapeutic data are summarised in table 1.

## **Discussion**

CO<sub>2</sub> laser treatment of severe LMO in SS patients was associated with significant improvement in mouth opening 3 months after the first laser session (mean +5 mm vs. baseline) with further improvement observed at 12 months (mean +8.5 mm vs. baseline). This improvement was clinically relevant and resulted in a reduction of mouth handicap as evaluated by the MHISS score.

The mechanism by which abrasive laser improves fibrosis in SS is not known. By analogy to what has been shown in the treatment of photoaging or scars, several hypotheses can be advanced. CO<sub>2</sub> laser could modulate the expression of transforming growth factor beta 1 [10], a major profibrotic mediator [11], resulting in normalisation of collagen balance. The abnormal increase in expression of collagen 1 in SS [12] may be modulated during CO<sub>2</sub> laser treatment [13] and a more homogeneous architecture of the dermis could be restored. CO<sub>2</sub> laser may also modulate the expression of VEGF, which is involved in the early stage of neo-collagenesis [14].

Treatment of LMO in SS is not standardised and there are limited treatment options. In 2011, an expert group proposed recommendations for the management of oral complications in SS [3]. The recommended treatment for LMO is based on stretching exercises for 3 months [3]. Pizzo et al. [15] reported a mean gain of +10.7 mm in IID after 18 months of stretching exercises. Another study reported a mean improvement of +5.7 mm of IID after 3 months of exercises [16]. There is limited standardisation of stretching exercises in terms of nature, frequency and duration. A minimum duration of 15 min twice a day is required [15]. They also need to be continued in the long term if the benefit is to be maintained [17]. Combination treatments including physiotherapy, massage and physical therapy may also improve mouth opening. The main limitation of these treatments is the lack of trained physical therapists. There are no data on the efficacy of CO<sub>2</sub> laser for the treatment of LMO. CO<sub>2</sub> laser treatment was evaluated in the management of perioral rhytids in patients with SS without any assessment of mouth opening [4] and was recommended by the expert group only for the treatment of perioral wrinkles [3]. Intense pulsed light treatment and perioral autologous fat injections have been advocated for the treatment of LMO. However, the reported efficacy was limited [18, 19].

The main limitations of our work are: the small number of patients treated. Better objective methods to assess clinical response for oral aperture in this condition in a multicentre setting are needed. Also, we understand the limitations in our work of the photographs which were performed without ruler. However, the evaluation of results has also included the MHISS scale, a validated scale in SS, and taken into account the patient perception. This confirms the clinical relevance of our findings. In addition, we did not assess intraoral sclerosis specifically.

In conclusion, CO<sub>2</sub> laser treatment of the white lips in SS seems to be an effective treatment of LMO. It is associated with improved mouth opening and patient quality of life.

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### Statement of Ethics

This article reports on a treatment procedure that is part of usual care for patients with skin diseases. It does not qualify as a study requiring ethical approval by an IRB in France. All patients signed a written informed consent for laser treatment.

## Disclosure Statement

The authors have no conflicts of interest to disclose. There was no funding for this work.

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**Table 1.** Demographic, clinical and therapeutic characteristics of patients

Patient characteristic	Patient 1	Patient 2	Patient 3	Patient 4
Sex	female	female	female	female
Age, years	57	63	43	45
Phototype	4	2	3	2
Type of SS	dSS	CREST syndrome	dSS	scleromyositis
Year of diagnosis	2007	1990	2008	1996
Modified Rodnan score (0–51)	17	18	12	15
Concurrent systemic disease	none	high blood pressure	none	none
Concurrent medications	nifedipine extended-release 30 mg/day	omeprazole 20 mg/day, alendronate 70 mg/month, irbesartan/hydrochlorothiazide 150/12.5 mg/day, amlodipine 5 mg/day	nicardipine 20 mg/day, hydroxy-chloroquine 200 mg/day, bosentan 125 mg × 2/day, 6 months/year iloprost infusion 0.5–1 ng/kg/min (6 h per day, for 5 days every 6–8 weeks), 6 months/year	diltiazem 60 mg × 2/day
Dates of CO <sub>2</sub> laser sessions	S1: 01/2012 S2: 11/2012 S3: 11/2013	S1: 04/2013 S2: 12/2013	S1: 01/2014	S1: 01/2014 S2: 11/2014
IID, mm	initial: 29 S1, M3: 34 S2, M3: 35 S3, M3: ND S3, M12: 36 final gain: +7 (24.1%)	Initial: 17 S1, M3: 24 S2, M3: 25 S2, M12: 27 final gain: +10 (58.8%)	initial: 26 S1, M3: 32 S1, M12: 35 final gain: +9 (34.6%)	initial: 25 S1, M3: 27 S2, M3: 30 S2, M12: 33 final gain: +8 (32%)
MHISS (0–48)	ND	initial: 44 final: 30	initial: 31 final: 14	initial: 42 final: 31
Patient global assessment of treatment response (–1, 0, +1)	+1	+1	+1	+1
Open question to patients: 'What is improved by this treatment?'	lip flexibility and easier dental care	lip flexibility and mouth opening with better phonation and mastication and easier dental care	mouth opening with better mastication and easier dental care	lip flexibility with better phonation and mastication and easier dental care
Adverse events (duration in days)	erythema: 15 pigmentation: 90	erythema: 15 pigmentation: 90	erythema: 15 hypochromia: 90	erythema: 15

dSS = Diffuse systemic scleroderma; S = session; M = month; ND = not done.



**Fig. 1.** Immediate appearance after pulsed CO<sub>2</sub> laser treatment in patient 4.





**Fig. 2.** First and second patients. **a** Mouth opening before CO<sub>2</sub> laser treatment in the first patient. **b** Mouth opening after the last evaluation in the first patient. **c** Mouth opening before CO<sub>2</sub> laser treatment in the second patient. **d** Mouth opening after the last evaluation in the second patient.





**Fig. 3.** Third and fourth patients. **a** Mouth opening before CO<sub>2</sub> laser treatment in the third patient. **b** Mouth opening after the last evaluation in the third patient. **c** Mouth opening before CO<sub>2</sub> laser treatment in the fourth patient. **d** Mouth opening after the last evaluation in the fourth patient.