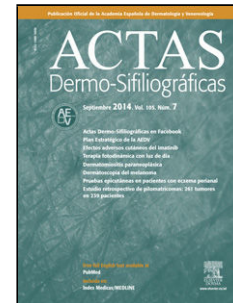


# Journal Pre-proof

Uso combinado de hialuronidasa y láser fraccionado ablativo y no ablativo para microstomía en 6 pacientes con esclerosis sistémica

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Carta científico-clínica

## Uso combinado de hialuronidasa y láser fraccionado ablativo y no ablativo para microstomía en 6 pacientes con esclerosis sistémica

[[Translated article]] Combined Therapy for Microstomia with Hyaluronidase and Ablative and Non-Ablative Fractional Laser in 6 Patients with Systemic Sclerosis

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*To the Editor,*

Microstomia is a common symptom in patients with systemic sclerosis (SS). Currently, there is no specific treatment, and it significantly impacts these patients' psychological well-being and quality of life.

In recent years, some very promising treatments have emerged, such as carbon dioxide (CO<sub>2</sub>) laser or the use of hyaluronidase. However, there is very little evidence regarding these. We are not aware of the use of non-ablative fractional laser in these cases or the combination of these therapies. We describe the cases of 6 patients with SS-related microstomia in whom the combination of hyaluronidase plus ablative or non-ablative fractional laser led to a significant improvement in oral aperture and high patient satisfaction.

Six women with SS and microstomia underwent subcutaneous hyaluronidase infiltration in small aliquots (approximately 5 to 10 units), using a 32 G needle periorally, maintaining an approximate distance of 0.5 cm between each injection point. Prior to administration, a negative hypersensitivity test on the forearm was required. The doses of hyaluronidase used varied between 300 IU and 660 IU, depending on the case treated. Immediately after, a session of ablative fractional CO<sub>2</sub> laser (Smart-Xide DOT®, Deka, Italy) or non-ablative fractional laser (NAFL) (ICON® 1540/IPL Cynosure platform) was performed, depending on each patient's preference for the subsequent recovery time, which varies between the 2. The parameters used were variable: using maximum powers of 19 W, 450 ms, and 800 dwell time for CO<sub>2</sub>, and 15 ms and 65 J for 1540. To evaluate treatment, maximum horizontal and vertical oral aperture was measured with a ruler in centimeters, as well as its impact on quality of life using the validated Mouth Handicap in Systemic Sclerosis (MHISS) scale at baseline and 2 months post-treatment. Photographs were taken, and patient satisfaction was assessed with a visual analog scale (VAS) from 0 to 10, where 10 was the maximum score.

The patients' characteristics are shown in Table 1. All were on immunosuppressive treatment for SS. A single session of hyaluronidase (doses varying between 300 and 660 IU) and a laser session immediately after were performed. Four patients received NAFL treatment, and 2 received ablative CO<sub>2</sub>. All patients showed improvement 1 month into therapy (Fig. 1): 5 improved oral aperture and 5 achieved a significant reduction in the MHISS scale (between 5 and 18 points difference). One patient's MHISS scale worsened, but the evaluation coincided with a worsening of her underlying lung disease, which we believe may be the reason. All patients were satisfied with the treatment, with scores between 8 and 10. Additionally, patients reported improved skin elasticity, reduced tightness sensation, as well as improved self-image and ease of dental hygiene. Patients did not experience any significant adverse effects.

Three patients have been followed for > 5 months, with sustained improvement.

Treatment of microstomia in SS is challenging. Typically, drugs used in clinical practice aim to improve visceral problems and inflammation, but they do not improve microstomia. This sign has many implications for patients' lives, including problems with adequate nutrition or performing regular proper dental care.

Hyaluronidase has emerged in recent years as a promising therapy because it plays a crucial role in the degradation of hyaluronic acid in the extracellular matrix. However, there are very few

reports on the subject: 2 are single cases and 2 are retrospective studies with 4 and 12 patients, respectively<sup>1-6</sup>. The number of sessions and doses used are highly variable in all of them (between 75 and 470 per session), and most have required > 1 treatment session (between 3 and 5). In our series, the dose of hyaluronidase used was higher, which, along with the subsequent use of laser, could explain why improvement was seen in all cases with a single treatment session. In all described cases, including ours, improvement occurred early.

On the other hand, CO<sub>2</sub> laser has been successfully used by authors such as Bennani et al., who performed between 1 and 3 sessions with good results<sup>7,8</sup>. To date, we have not found any reference on the use of NAFL and microstomia. The mechanism by which laser acts is not fully understood. In a clinical trial, Taudorf et al.<sup>9</sup> observed an improvement in the thickness and flexibility of burn scars, as well as a normalization of collagen at the histological level 6 months into therapy. Furthermore, it appears to modulate the expression of beta factor (a profibrotic mediator), resulting in a normalization of collagen imbalance. Additionally, CO<sub>2</sub> could modulate the increase of type I collagen and VEGF expression, which is involved in initial stages of neocollagenesis.

Either one of the 2 lasers used can induce dermal remodeling, with greater effect from ablative lasers, which is why we believe their use likely offers more benefit<sup>10</sup>. The main difference between the 2 lies in skin recovery time, which is longer for ablative lasers, leading some patients to prefer the non-ablative option.

According to our results, we believe that the combined technique can offer benefits compared to the isolated use of techniques. On the one hand, because the heat generated by the laser can help diffuse the previously injected hyaluronidase, and because the mechanism of action of the 2 techniques is different and complementary<sup>11,12</sup>.

The limitations of this study are mainly the sample size and the lack of a control group with single therapy.

We believe that combined treatment with hyaluronidase and laser is an effective and safe alternative for the treatment of microstomia in patients with SS. In our experience, it improves oral aperture, associated symptoms, and patients' self-esteem.

## Conflicts of interest

None declared.

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**Figure 1.** Patients treated with hyaluronidase and laser showed improved oral aperture diameter and visible teeth in frontal views. From a lateral perspective, greater skin retraction was observed when opening the mouth after treatment.



**Table 1.** Patients with SS Treated with Hyaluronidase and Consecutive Laser Therapy

Patient	Condition	Total Hyaluronidase Dose	Laser Used	Initial Size	Final Size	Initial MHISS	Final MHISS	VAS	Other Comments
1	MCTD (SS + LE)	—	1540	—	—	35	25	10	Improved feeding
2	SS	450 IU	1540	4 × 4.1 cm	4 × 4.3 cm	29	24	10	Improved skin elasticity, easier dental procedures
3	SS	300 IU	1540	3.5 × 3.3 cm	4.5 × 4.5 cm	29	35	—	Improved cheilitis
4	SS	660 IU	1540	5 × 4.4 cm	5 × 4.4 cm	24	13	8	Improved sensitivity, less hardness, more elastic skin
5	SS	650 IU	CO <sub>2</sub>	5.5 × 4.5 cm	4.7 × 3.8 cm	27	9	10	Less tightness, fewer wrinkles
6	SS	650 IU	CO <sub>2</sub>	5.2 × 4.6 cm	5.4 × 5 cm	29	15	8	Improved sensitivity in the area

CO<sub>2</sub>, carbon dioxide; MCTD, mixed connective tissue disease; SS, systemic sclerosis; LE, lupus erythematosus; VAS, visual analogue scale; MHISS, Mouth Handicap in Systemic Sclerosis