

Collagenase as a Therapeutic Approach for Secondary Microstomia in Patients with Systemic Sclerosis: A Case Series

Natacha Quezada Gaón^{1*} and Joaquín Peñaloza²

¹Department of Dermatology, Faculty of Medicine, Pontificia Universidad Católica de Chile, Dermaline Clinic, Santiago, Chile

²Medical Student, Faculty of Medicine, Universidad Finis Terrae, Santiago, Chile

***Corresponding author:** Natacha Quezada Gaón, Department of Dermatology, Faculty of Medicine, Pontificia Universidad Católica de Chile, Dermaline Clinic, Santiago, Chile, Tel: +56 2 2633 2051; E-mail: natachaq@yahoo.es

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1. Introduction

Systemic Sclerosis (SSc) is a chronic connective tissue disease with an estimated prevalence ranging from 17.6 to 18.9 cases per 100,000 individuals, affecting approximately 1 in every 5,300 people [1].

Microstomia is a common and disabling manifestation of systemic sclerosis, resulting from progressive dermal fibrosis associated with decreased matrix metalloproteinase-1 (MMP-1) activity and excessive collagen accumulation. Microstomia significantly impairs oral function, leading to difficulties with food intake, speech, and oral hygiene.

It also exerts a considerable negative impact on facial aesthetics and quality of life. Consequently, once SSc has reached clinical stability, therapeutic interventions aimed at improving oral and restoring facial function should be considered.

The collagenase used to treat Peyrone's disease has been shown to selectively degrade collagen fibers, weakening the fibrotic plaque and allowing tissue remodeling [2]. Additionally, collagenase in injections have also shown to degrade collagen fibers [3,4].

Herein we report 3 cases of Female patients with microstomia secondary to SSc treated with collagenase:

Patient 1: 51-years-old Female with diagnosis of SSc for 15 years in immunosuppressive treatment with prednisone and mycophenolate, stable for 5 years.

Patient 2: 54-years-old Female with diagnosis of SSc, Systemic Lupus, and hypothyroidism for 12 years in immunosuppressive treatment with tacrolimus and mycophenolate with stable clinical conditions for 6 years.

Patient 3: 58-years-old Female with diagnosis of SSc for 10 years in immunosuppressive treatment with mycophenolate, stable for 3 years.

2. Materials and Methods

Systemic Sclerosis (SSc) is characterized by excessive extracellular matrix deposition, fibrosis, microvascular dysfunction, and progressive tissue stiffening.

Recombinant enzymes (*PBSerum*) were planned for use as follows: **5 mL of Collagenase** (degrades collagen-rich fibrotic septal, softens dense connective tissue), 1 mL of Hyaluronidase (reduces extracellular matrix viscosity, improves tissue permeability and facilitates the diffusion of collagenase), 1 mL of Lipase (may enhance the activity of collagenase and hyaluronidase indirectly by facilitating tissue remodeling.), and 1 mL of Lidocaine without vasoconstrictor. The recombinant enzymes each enzyme targets a distinct component of the extracellular matrix or adipose tissue.

Standardized photographs were obtained before and directly after the procedure, both at rest and during maximal mouth opening. The amplitude of mouth opening was measured using a ruler, in cm. Sclerotic bands that were visible and palpable in the perioral region were identified and marked at 1.5 cm intervals prior to treatment.

Following facial asepsis and antisepsis, the enzyme solution was administered into the subcutaneous plane at a dose of 0.2 mL per injection point. Subsequently, vigorous massage of the treated area was performed, as an almost immediate clinical effect was observed. Representative clinical photographs were obtained before and after treatment (FIG. 1-3).



FIG. 1. Marking of application points on visible and palpable fibrotic bands.



FIG 2. Clinical photograph at rest before (A) and after (B) collagenase application.

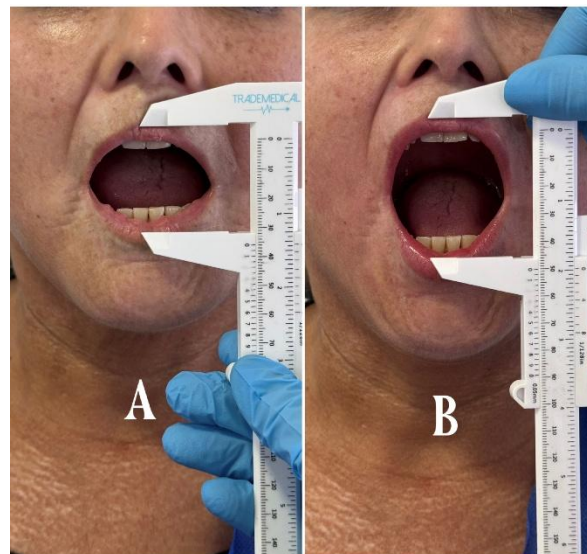


FIG. 3. Clinical photograph showing mouth opening before (A) and after (B) collagenase application.

Given the favorable clinical outcomes, we conducted this case series using a single treatment session. However, we anticipate that some patients may require multiple sessions.

3. Results and Discussion

All three patients demonstrated a reduction in the stiffness of perioral fibrotic bands and an increase in maximal mouth opening of 1.0 cm, 1.2 cm, and 1.1 cm, respectively. These improvements remained stable throughout the 6-month follow-up period (through new measurements) and were associated with enhanced quality of life, particularly with respect to eating and oral hygiene. Regarding adverse effects, one patient developed transient ecchymosis, while no cases of edema were observed.

In addition, no increase in the activity of the underlying disease was detected in any of the three cases (FIG. 4). Previously reported treatments for microstomia have included hyaluronic acid fillers, which have been shown to improve both lip aesthetics and patients' quality of life [5]. To the best of our knowledge, no prior studies have shown the use of collagenase in microstomia.

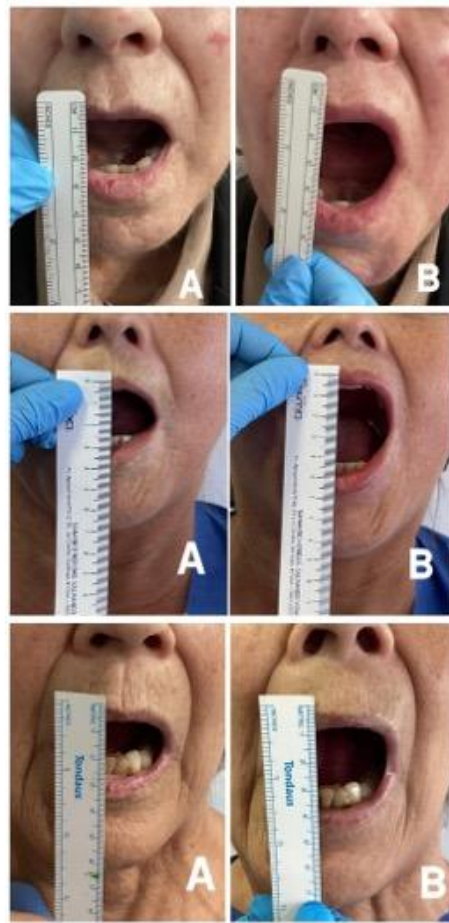


FIG .4. Mouth opening before (A) and after (B) collagenase application.

Our findings suggest that collagenase may serve as a useful preparatory step before filler or botulinum toxin injection, as it appears to increase the distensibility of fibrotic tissue and facilitate subsequent filler placement. The main limitation of this case series is the small sample size, which is planned to be expanded in future studies.

4. Conclusion

Collagenase is a useful treatment for microstomia in patients with SSc, improving quality of life through a simple and reproducible technique. We believe our findings provide valuable preliminary clinical evidence and may stimulate further prospective research.

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