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ORIGINAL ARTICLE

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Efficacy of photo-thermal-bioactivated platelet-rich plasma for skin biostimulation in patients not eligible for other medical-aesthetic treatment: A pilot study

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Abstract

Purpose: To evaluate the efficacy and safety of photothermal bioactivated platelet-rich plasma for reducing laxity in facial rejuvenation in patients not eligible for other aesthetic treatments due to several comorbidities.

Methods: A prospective, nonrandomized study was conducted. Efficacy was assessed through a satisfaction scale and the Facial Laxity Rating Scale. Safety assessments were based on the data of all adverse events and the visual analog pain scale.

Results: Seven patients with a mean age of 51 (standard deviation [SD] 7.46, range 42–63) were included. In six patients (85.7%), the treatment was applied to the face and neck, and in one patient (14.3%), only to the lower half of the face and neck. The physician's perception of laxity decreased, and the procedure was not complex. Patients' and physician satisfaction increased as the study progressed. Adverse effects were not serious and resolved without sequelae. The patients' pain perceived during the treatment was mild in most cases.

Conclusion: The photothermal bioactivated platelet-rich plasma injections were a safe and effective treatment for facial laxity in patients not eligible for other procedures, providing good satisfaction.

KEYWORDS
aging, growth factors, laxity, photothermal bioactivated platelet-rich plasma, rejuvenation

1 | INTRODUCTION

Facial aging is a biological process influenced by endogenous factors, such as genetics, hormone, and metabolic processes, and exogenous factors, such as pollution or chronic sun exposure.[1–3] Aging involves skeletal changes, with a loss of volume in the fatty compartment and changes in skin components, such as the loss of dermal collagen and elastic fibers.[4] These changes affect external appearance and self-esteem due to losing a more youthful and attractive appearance.[5] The skin becomes thinner and loses elasticity, leading to sagging.[6]

There are various procedures and approaches for treating and preventing skin aging, such as topical agents, chemical peels or visible light devices, systemic agents like hormone replacement therapy, and correction of lifestyle and habits like smoking or nutrition, diet restriction, and alimentary supplementation.[7]

Skin bio-rejuvenation aims to increase fibroblasts' biosynthetic capacity, achieve reconstruction, improve cell activity and hydration, and synthesize collagen, elastin, and hyaluronic acid (HA). Among facial treatments, the most widespread are fillers through which products are injected in or under the skin to improve physical characteristics

by increasing soft tissue and whose effect is temporary.[8,9] The most widely used products are fillers with stabilized or viscoelastic nonanimal HA from bacterial fermentation and autologous platelet-rich plasma (PRP). PRP is obtained from the patient's whole blood, extracted just before the application of the treatment, and contains a high concentration of platelets, growth factors such as epidermal growth factor (EGF), basic fibroblast growth factor (bFGF), platelet-derived growth factor, transforming growth factor, vascular endothelial growth factor (VEGF), and insulin-like growth factor.[10] These factors are secreted from α granules of concentrated platelets and activated by aggregation inducers.[11] They can regulate processes such as cell migration, attachment, proliferation, and differentiation and promote the accumulation of extracellular matrix by binding to specific cell receptors on the cell surface.[12] It has been shown that PRP can induce the synthesis of collagen and other matrix components, stimulating the activation of fibroblasts and rejuvenating the appearance of the skin.[13,14] However, there is limited knowledge of how they intervene concerning aging. PRP therapy is generally well tolerated and suitable for all phototypes[15] and even is used for treating patients with various dermatological conditions and concerns. Photothermal-bioactivated PRP (PTBA-PRP) is currently being used for facial rejuvenation with excellent results.[16]

The study's objective was to evaluate the efficacy and safety of photothermal bioactivated platelet-rich plasma for reducing laxity in facial rejuvenation in patients not eligible for other aesthetic treatments due to several comorbidities.

2 | MATERIALS AND METHODS

2.1 | Study design and participants

A prospective, single-center, nonrandomized study was carried out to assess the efficacy and safety of PTBA-PRP for skin biostimulation of the face and neck to reduce laxity caused by aging in patients not eligible for other medical-aesthetic treatments. The study was conducted at Arts Clínic (Valencia, Spain).

The study was conducted following the principles outlined in the revised version of the Declaration of Helsinki, Good Clinical Practice, and compliance with all applicable laws and regulatory requirements relevant to sanitary products in Spain. All patients signed the informed consent for participation. Data collection and management were carried out following the laws on protecting natural persons concerning the processing of personal data and the free movement of such data.

2.2 | Selection criteria

The women included had to be between 35 and 75 years old with comorbidities for which other more aggressive medical aesthetic treatments were not recommended. Patients with skin infections in the area to be treated were excluded.

TABLE 1 Patients' baseline characteristics.

	Total, $N = 7$
Sex, *n* (%)	
Women	7 (100%)
Age, mean (SD)	51 (7.46)
Body Mass Index, mean (SD)	22.2 (1.89)
Lifestyle and habits, *n* (%)	
Smoking	1 (14.3%)
Cosmetical care	7 (100%)
Sun exposure	4 (57.1%)
Sleep pattern	5 (71.4%)
Disease*, *n* (%)	
Fibromyalgia	1 (14.3%)
Rheumatoid arthritis	1 (14.3%)
Breast cancer	1 (14.3%)
Autoimmune thyroiditis	2 (28.6%)
Hypercholesterolemia	1 (14.3%)
Permanent implant	3 (42.9%)
Myasthenia gravis	1 (14.3%)
Pharmacological treatment	
Vandral, diazepam, noctamid	1 (14.3%)
Tramadol, phenylbutazone, nolotil	1 (14.3%)
Humira, methotrexate, acfol, saxenda	
Ezetrol, eutirox, orfidal	1 (14.3%)
Eutirox, finasteride	1 (14.3%)
Experimental vaccine	1 (14.3%)
No medication	2 (28.6%)

*Several patients could have several diseases.

2.3 | Visits and treatment procedures

Several visits were carried out: a baseline visit (V1), at 7 days (V2), at 21 days (V3), and 42 days (V4). Treatment was applied to the face and neck.

PTBA-PRP was prepared in two easily identifiable steps: Standard PRP grafting procedure and photothermal stimulation of PRP. For the standard PRP grafting procedure, closed blood processing systems were used to collect 30 mL of autologous blood, samples were centrifuged at 3500 rpm for 5 min, platelets were separated from red and white blood cells, and 10 mL of PRP was obtained. For the photothermal stimulation of PRP, the sample was placed in an MCT Kit (Metacell Technology, Sant Cugat, Spain), a sterile 10 mL single-use container manufactured with a medical-grade special polymer. Samples were then stimulated with light and temperature using MCT Unit (Metacell Technology, Sant Cugat, Spain). The protocol exposed the samples to 623-nm light 5.6 J and 4°C simultaneously.

PTBA-PRP was injected superficially, 0.05 mL per prick. For the "point-to-point" mesotherapy technique, a 30G½ needle was used at

TABLE 2 Before each procedure, the doctor assessed the laxity through the facial laxity rating scale (FLR).

Laxity assessment with the facial laxity rating scale (FLR)			
	Face upper half Doctor	Face lower half Doctor	Neck Doctor
Patient 1 (54 years)			
Visit 1	6	5	5
Visit 2	5	5	5
Visit 3	3	3	2
Visit 4	3	3	2
Laxity class reduction	3	2	3
Laxity grade reduction	1	1	1
Patient 2 (42 years)			
Visit 1	5	5	6
Visit 2	3	4	4
Visit 3	–	3	4
Visit 4	3	2	2
Laxity class reduction	2	3	4
Laxity grade reduction	1	1	1
Patient 3 (52 years)			
Visit 1	7	8	5
Visit 2	5	5	5
Visit 3	4	3	4
Visit 4	3	2	3
Laxity class reduction	4	6	2
Laxity grade reduction	2	2	1
Patient 4 (55 years)			
Visit 1	6	6	6
Visit 2	5	5	4
Visit 3	4	4	4
Visit 4	4	3	3
Laxity class reduction	2	3	3
Laxity grade reduction	0	1	1
Patient 5 (63 years)			
Visit 1	7	8	6
Visit 2	6	6	5
Visit 3	5	4	5
Visit 4	5	3	4
Laxity class reduction	2	5	2
Laxity grade reduction	1	2	0
Patient 6 (42 years)			
Visit 1	4	4	4
Visit 2	3	2	2
Visit 3	3	2	2
Visit 4	2	2	1
Laxity class reduction	2	2	3
Laxity grade reduction	1	1	1
Patient 7 (56 years)			
Visit 1		6	6
Visit 2		5	5
Visit 3		4	3
Visit 4		4	3
Laxity class reduction		2	4
Laxity grade reduction	–	0	1

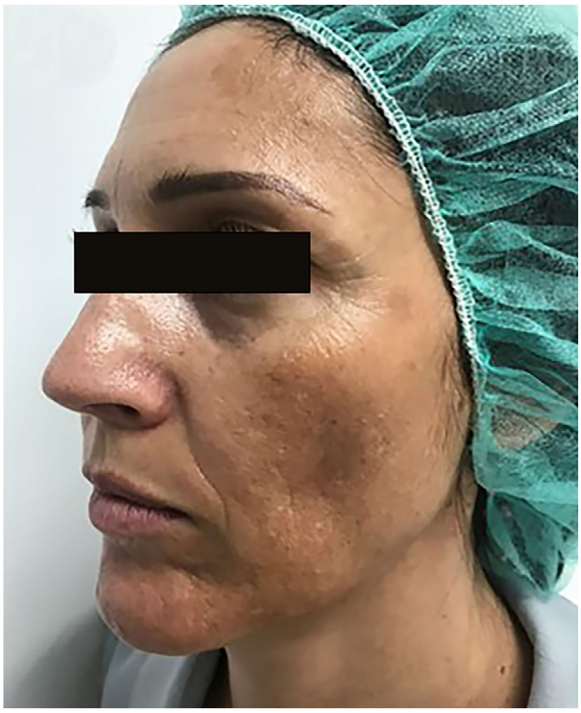

FIGURE 1 Patient 6 (42 years old), before PTBA-PRP facial treatment.

a depth of 2.0 mm. The amount of PTBA-PRP injected was 8–10 mL distributed over the face or the neck.

2.4 | Treatment and efficacy endpoint and variables

Data were collected on age, weight, height, BMI (kg/m^2), smoking habit, daily cosmetic care (yes, no), sun exposure (low = 0, medium = 1, high = 2), use of a daily sun protection factor (SPF) (yes, no), hours of sleep ≥6 (yes, no), concomitant conditions and medications.

For the efficacy analysis, all sessions were evaluated by the doctor and patients independently, using a questionnaire designed for the study. Before and after each session, photographs of the treated

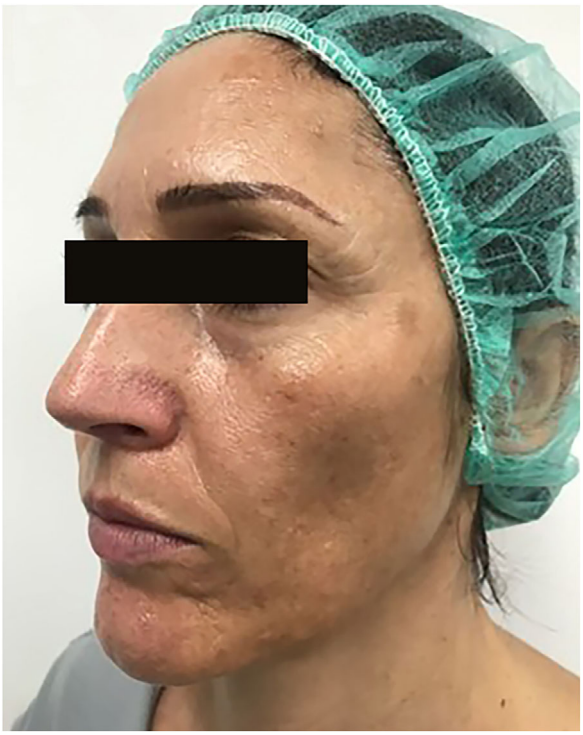

FIGURE 2 Patient 6 (42 years old), after PTBA-PRP facial treatment.

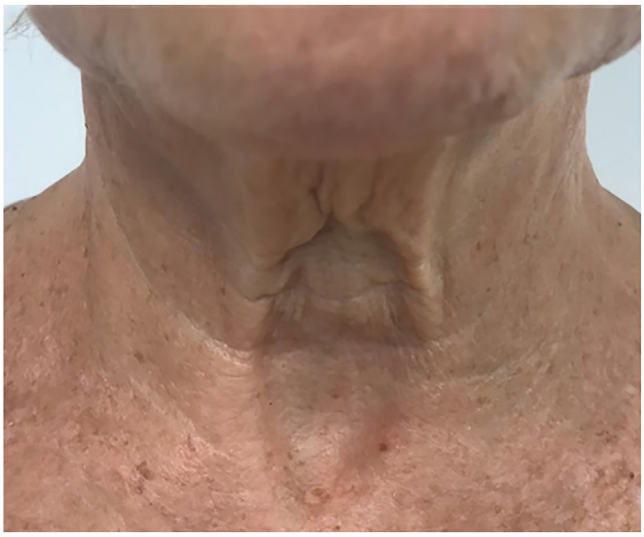

FIGURE 3 Patient 5 (63 years old), before PTBA-PRP neck treatment.

area were taken. The efficacy assessment was performed by evaluating three scales that objectively reflected the results achieved and subjectively the patients' level of comfort and satisfaction.

The treatment satisfaction scale evaluated the doctor and patient's satisfaction with the procedure and results. It was assessed at the end of the treatment. The response was based on a Likert scale (from 1 to 7) where 1 = fully satisfied, 2 = moderately satisfied, 3 = slightly satisfied, 4 = no changes noticed, 5 = slightly unsatisfied, 6 = moderately unsatisfied, and 7 = fully unsatisfied.

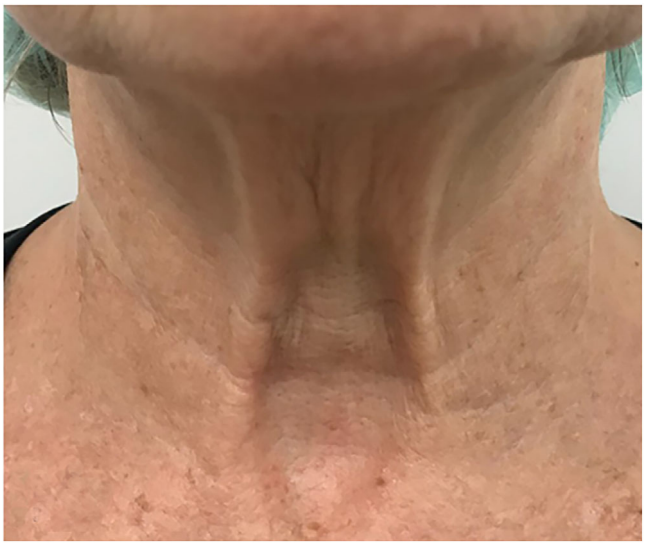

FIGURE 4 Patient 5 (63 years old), after PTBA-PRP neck treatment.

Visual analog scale (VAS) was used to assess the pain perceived by the patients during the treatment. VAS has 11 degrees, where 0 = no pain, 2 = mild pain, 4 = moderate pain, 6 = severe pain, 8 = very severe pain, and 10 = maximum imaginable pain.

The doctor used the facial Laxity Rating Scale (FLR) to assess facial laxity. This scale divides the face into four regions: upper face (eyelid fold), middle face (nasojugal fold), lower face (jowls), and neck (neck angle).[17] The assessment was performed before each session. FLR scale includes three degrees of laxity: mild, moderate, and severe, and each of them is subdivided into three classes: 1, 2, and 3 (mild); 4, 5, and 6 (moderate); and 7, 8, and 9 (severe). The reduction in classes and the laxity degree were calculated in each treated area (upper half of the face, lower half of the face, and neck) at the end of the treatment.

2.5 | Safety assessments

Safety was assessed by asking patients if they had experienced complications or adverse effects (AEs) during treatment administration or between visits, to which the answer could be "no" or "yes." If the answer was "yes," they had to specify whether it was pain, erythema (redness), bruising, nodules, or other. If responding to others, they were asked to describe them. Data on the type of AEs, appearance date, duration, degree, and measures adopted in each case were collected.

2.6 | Statistical analysis

Statistical analysis included quantitative variables as the mean and standard deviation (SD), whereas categorical variables were described as frequency or percentage.

TABLE 3 Patients' and doctors' satisfaction level with the results obtained in each treatment visit, adverse events, and pain perceived during the study.

	Global satisfaction			Safety assessments (adverse events)				
	Physician	Patient	Treatment VAS	Pain	Erythema	Hematoma	Nodules	Edema
Patient 1 (54 years)								
Visit 1			2		X			
Visit 2	3	4	2					
Visit 3	1	2	2					
Visit 4	2	1	2					
Patient 2 (42 years)								
Visit 1			4		X			X*
Visit 2	3	4						
Visit 3	2	3	2		X			X**
Visit 4	2	4						
Patient 3 (52 years)								
Visit 1			2	X	X	X		
Visit 2	2	2	2					
Visit 3	2	3	2			X		
Visit 4	2	1	2			X		
Patient 4 (55 years)								
Visit 1			4					
Visit 2	2	4	2	X		X		
Visit 3	3	3	2	X				
Visit 4	2	3	3					
Patient 5 (63 years)								
Visit 1			4			X		
Visit 2	2	4	4					
Visit 3	2	4	4					
Visit 4	2	1	4					
Patient 6 (42 years)								
Visit 1			2		X			
Visit 2	1	2	1		X			
Visit 3	1	2	1		X			
Visit 4	2	1	3					
Patient 7 (56 years)								
Visit 1			2			X		
Visit 2	3	4	2					
Visit 3	1	3	2					
Visit 4	2	2	1					

Abbreviation: VAS, visual analog scale.
*Severe: Face and neck.
**Face and oval of the face.

3 | RESULTS

3.1 | Subject characteristics

Seven patients with a mean age of 51 (SD 7.46, range 42 to 63) and a mean BMI of 22.1 (SD1.9) were included. Six patients (85.7%) received PTBA-PRP treatment on the face and neck, and one (14.3%) on the lower half of the face and neck. Six patients completed the four treatment visits, and one patient, who underwent a full face and neck treatment, completed two treatment visits. Baseline data are detailed in Table 1.

3.2 | Primary efficacy outcomes

The laxity values given by the doctor before each visit are collected in Table 2. All patients achieved a reduction in the laxity class in any treated area. Six patients were treated in the upper half of the face: one patient showed laxity reduction from severe to mild, lowering from 7 to 3 on the FLR scale; four patients showed laxity reduction from moderate to mild, reducing their scores on the FLR scale from 6 to 3, from 5 to 3, from 7 to 5, and from 4 to 2; one patient showed laxity reduction within the moderate degree, showing a reduction from 6 to 4 in the FLR scale. Seven patients were treated in the lower half of the face: two patients showed laxity reduction from severe to mild, reducing their scores on the FLR scale from 8 to 2 and from 8 to 3); four patients showed laxity reduction from moderate to mild, reducing their scores in the FLR scale from (from 5 to 2, from 6 to 3, from 5 to 3, and from 4 to 2); one patient showed laxity reduction within the moderate degree, showing a reduction from 6 to 4 in the FLR scale. In the neck area, seven patients were treated: all of them showed laxity reduction from moderate to mild, reducing their scores in the FLR scale from 6 to 2 in two cases, from 5 to 2, from 6 to 3, 4 to 1, and from 5 to 3 in two cases. Examples of two patients before and after the complete PTBA-PRP treatment are Figure 1, patient 6 (42 years old), before facial treatment; Figure 2, patient 6 after treatment; Figure 3, patient 5 (63 years old) before neck treatment; and Figure 4, patient 5 after treatment.

Physician and patient satisfaction after the treatment is in Table 3. The degree of satisfaction was good at every session. Patient and physician satisfaction assessments were coincident in 65% of the cases.

3.3 | Safety findings

AEs occurred, and pains perceived during the study are listed in Table 3. AEs were scarce and mild, except for one patient who had an allergic or *a frigore* reaction with facial edema and required Methylprednisolone (Urbason 16 mg) for a standard and *ad integrum* resolution. In the second session, she presented the same reaction with face and neck edema, though much less severe.

4 | DISCUSSION

This pilot study showed a decrease in laxity after PTBA-PRP treatment. All patients had a reduction in the laxity class, and 84.5% achieved, at least, a reduction of one level in the laxity grade. The product was safe, and the photothermal bioactivation procedure presented no technical problems. Side effects were scarce and resolved. Patients' perceived pain was considered mild in 57.7% ($n = 15/26$) of the sessions. The good satisfaction level referred by the patients and the physicians increased even further as the treatment progressed.

Studies on thermal and photo-activated PRP had reported results in which EGF, bFGF, and VEGF concentrations were significantly increased after thermal biomodulation (TBM) protocols.[18] Other studies have shown that the thermoactivated PRP, maintaining high quality, showed more physiological characteristics than PRP without additives.[19] A comparative study with PTBA-PRP in the aging facial treatment following the same preparation protocol and device of our study,[16] rated skin improvement as good as 60%, compared to the one obtained with PRP without PTBA. None of them reported severe AEs and or technical issues. In comparison to nonphotothermal-biostimulated PRP, patients perceived the "most noticeable change in skin quality" as being more radiant/luminous (27.4%), while others referred to better-overall results (16.4%) or a smoother appearance (15.1%).

In addition to the limitations associated with its nonrandomized design, another limitation was the small number of patients included because we wanted to conduct a pilot study due to the scarce evidence available with this technique and the special characteristics of the subjects that conformed to the sample. However, the data obtained will help to increase the knowledge of this technology and its various applications.

5 | CONCLUSION

The photothermal bioactivated platelet-rich plasma injections were a safe and effective treatment for facial laxity in patients not eligible for other procedures, providing good satisfaction.

CONFLICT OF INTEREST STATEMENT

Carlota Hernández has no conflict of interest or financial ties to disclose. Hernán Pinto is a scientific consultant for Clinipro, a manufacturer of MCT; however, has not received any fee for this study. The authors thank all their collaborators and the i2e3 Biomedical Research Institute medical writing team for their collaboration.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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