



# Efficacy and Safety of Autologous Platelet Concentrate in the Treatment of Photoaging on the Back of the Hands



Israel Alfonso Trujillo\*, Yetter Cruz Leon, Charllonne Angelica Marte Arias, Yaquelin Luciana Morales Novo, Jesus Lazaro Diego De la Campa, Angela Rosa Gutierrez Rojas, Julio Antonio López Silva and Daymi Serpa Almaguer

Clinical Surgical Hospital Hermanos Ameijeiras, Cuba

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\*Corresponding author: Israel Alfonso Trujillo, Clinical Surgical Hospital Hermanos Ameijeiras. Havana, Cuba

## Abstract

**Introduction:** From the fourth decade of life (especially on the back of the hands) the skin becomes dry and brittle, spots appear, the venous network increases and soft tissues decrease.

**Objective:** To evaluate the efficacy and safety of intradermal microinjection of autologous platelet concentrate (APC) in the treatment of rejuvenation of the back of the hands.

**Method:** An observational, analytical and longitudinal study was carried out in 60 patients from the Hospital Clínico Quirúrgico: "Hermanos Ameijeiras", in the period between March 1, 2017 and March 31, 2020. The treatment was applied monthly for 1 year. The final evaluation was carried out 3 months after the end of the treatment.

**Results:** 51 women with an average age of  $45 \pm 4.3$  years were treated. After treatment, there were significant changes in the Glogau photodamage scale ( $p = 0.012$ ), in the global scale of aesthetic improvement ( $p < 0.001$ ) and in the scale of the degree of involvement of the volume of the hand ( $p = 0.018$ ). The adverse events found were pain, inflammation and ecchymosis. The degree of satisfaction reported by the patients was good (26.6%) and very good (73.4%) ( $p < 0.001$ ).

**Conclusion:** The autologous platelet concentrate proved to be effective and safe in reducing the signs of cutaneous aging on the back of the hands, associated with a high degree of patient satisfaction.

**Keywords:** Platelet-rich plasma; Rejuvenation; Photoaging; Autologous platelet concentrate

## Introduction

From the fourth decade of life, the skin becomes dry and brittle, spots appear, red vein increases and soft tissues decrease, especially on the back of the hands. To achieve rejuvenation of the hands, the aesthetic doctor must combine and adapt various treatments. Platelet-rich plasma (PRP) and its growth factors (GF) have a recognized revitalizing, regenerative and biorepairing effect, [1,2] however few studies objectively evaluate their efficacy, which led to the realization of the present investigation.

## Goals

The primary objective was: to determine the effectiveness and safety of the microinjection of autologous platelet concentrate

(APC) in the treatment of photoaging of the back of the hands and the secondary objectives were: 1) to evaluate the clinical response to treatment, 2) to evaluate type and intensity of adverse events that occur and 3) describe the degree of patient satisfaction.

## Method

An observational, analytical, longitudinal study was carried out in 60 patients at the Hospital Clínico Quirúrgico: "Hermanos Ameijeiras", in the period between March 1, 2017 and March 31, 2020. Treatment with APC was applied monthly for 12 months. Three months after the end of the treatment, the response to it was sent (final evaluation), comparing the current state (soft tissues, veins, tendons and skin) with the initial state; for this, the

patient had to attend the scheduled consultation. Throughout the study there was a rigorous control of adverse reactions. Before and after proceeding, the platelets were quantified to know the quality of the applied product (the average concentration of the platelets after advancing 10.8 times its initial value). Microbiological culture of the extracted plasma was performed to guarantee that a sterile germ product was administered.

**Inclusion criteria**

Patients between 20 and 60 years old, of any sex and skin phototype, skin photoaging grade II, III and IV (Glogau classification) (Table 1), [3] grade 1 to 3 according to scale of the degree of affection of the volume of the (HVRS) (Table 2), [4] normal complementary tests (hemogram with differential, coagulogram, blood chemistry and serology for HIV, hepatitis B and C), with signed informed consent.

**Table 1:** Classification of photoaging according to Glogau [3].

Type	Characterization
Type I "No wrinkles"	Early photoaging: slight pigmentary changes, no keratosis, minimal wrinkles, no scars, young patient, generally 28-35 years of age, no or minimal makeup.
Type II "Movement wrinkles"	Early to moderate photoaging: visible early senile lentigo, early actinic keratosis, slight signs of scars, wrinkles and parallel smile lines begin to appear; patient age: late 30s or 40s, usually she wears some makeup.
Type III "Wrinkles at rest"	Advanced photoaging: obvious dyschromia and telangiectasias, visible keratoses, neoplasms (+), wrinkles even when not moving, patient age: fifty years or older, always wears a lot of makeup.
Type IV "Wrinkles only"	Intense photoaging: grayish-yellow skin, cutaneous neoplasms (+++), all wrinkled skin, no normal skin, age of patient: sixties or seventies, cannot wear makeup, "hard and cracked".

**Table 2:** Hand volume involvement scale (HVRS) [4].

Grade		Characteristics
0	Absent	No loss of soft tissue, veins not visible or only superficially visible and no visible tendons.
1	Minimal	Minimal soft tissue loss, only slightly prominent and visible or no tendons.
2	Moderate	Moderate loss of soft tissue, prominent veins, and markedly visible tendons.
3	Moderately severe	Moderately severe soft tissue loss, very prominent veins, substantially protruding tendons (most tendons visible), rough skin, and presence of fine wrinkles. All the aforementioned conditions are mandatory.
4	Severe	Severe soft tissue loss, markedly prominent veins, extremely protruding tendons (all tendons visible), very rough skin with dermal atrophy, and severe presence of fine wrinkles. All the aforementioned conditions are required.

**Exclusion criteria (Table 3)**

**Elimination criteria**

Patients who wish to abandon the study, presence of an adverse event and / or complication that prevents continuing with the treatment or patients who have missed a treatment session.

**Procedures**

Once the patients gave informed consent, the included subjects registry template and the investigator’s internal registry were filled out. All information on the included patients was compiled in the data collection notebook. The blood was extracted (500 milliliters), then the APC was obtained with the Rotixa centrifuge (221 mm radius) according to international standards [5]. To obtain the APC, a first light centrifugation of the whole blood

was carried out in the plastic bag for 3 minutes at 2800 rpm at 22 °C, with a centrifugation force of 2000 g, in this way 250 ml of red blood cells and 250 ml were obtained of PRP; then a second weighted centrifugation was performed on the PRP in the plastic bag for 5 minutes at 4500 rpm at 22 °C, with a centrifugation force of 5000 g. Once the heavy centrifugation had been carried out, the supernatant plasma was transferred through the tubes that have the plastic bags for blood collection and only 10 ml were left and it is in said volume that by shaking the platelets that were deposited in the cell were resuspended. bottom of the bag as results of the centrifugation procedure. Subsequently, the red blood cells were returned to the patients and finally a microinjection of 10 milliliters of the APC was performed, distributed between the back of the hands, the entire facial area, V of the décolleté and neck.

**Table 3:** Exclusion criteria and their relationship with the time limits to perform the procedure.

Criteria	Time limits
Congenital or acquired coagulation disorders.	Prior and simultaneous to the procedure
Bone marrow aplasia.	Prior and simultaneous to the procedure
Prone to forming keloids.	Before the procedure
Cardiovascular or pacemaker, neurological, liver, kidney, endocrine or immunological diseases, decompensated.	Simultaneous to the procedure
Severe psychiatric disorder or other limitation that prevents the patient from giving his informed consent or makes his evaluation difficult.	Simultaneous to the procedure
Pregnancy or breastfeeding	Simultaneous to the procedure
Treatment with anticoagulants, antifibrinolytics, macrolides, terfenadine, cimetidine, amiodarone, fluoxetine, NSAIDs, or corticosteroids.	One month prior to the procedure
Application of topical retinoids, aesthetic treatments in the region to be treated, including lasers, intense pulsed light, chemical peels, mesotherapy, carboxytherapy or others.	Three months prior to the procedure
Fillers in the region to be treated.	One year prior to the procedure
Active neoplastic diseases or during the follow-up period	Five years post-healing prior to the procedure

Asepsis and antisepsis of the back of the hands were performed. Radial and ulnar nerve block was performed by subcutaneous infiltration of 3 ml of 2% lidocaine close to the styloid process of the radius (anatomical tobacco box) and another 3 ml of 2% lidocaine at the level of the styloid process of the ulna (between the flexor carpi ulnaris tendon and the ulnar artery). Once the APC was activated with 10% calcium gluconate (concentration 10:1), it was administered by combining cannulas and needles. Punctures were made with a 20G needle at the level of the dorsal surface of the second, third and fourth interdigital spaces and through these punctures a 1 mm × 10 cm long cannula with a blunt tip was introduced, with which the APC was administered by

subcutaneously (fan and backtracking techniques). Subsequently, with a 25G × 16 mm hypodermic needle and 1 ml syringes, intradermal injections of approximately 1.5 ml were administered at a distance of 1.5 to 2 mm between each application area (point-to-point, fan, backtrace and nappage).

**Variables related to the response to treatment**

The response to treatment was evaluated taking into account the clinical examination of the patient, using the Glogau photodamage scale (Table 1),[3] the global aesthetic improvement scale (GAIS) (Table 4)[6] and the scale of the degree of involvement of the volume of the hand (Table 2)[4].

**Table 4:** Global aesthetic improvement scale (GAIS) [6].

Evaluation		Degree of improvement
1	Total answer	Patient with exceptional or much better improvement (excellent corrective result, total disappearance of the lesions).
2	Marked partial response	Patient greatly improved or considerably better (marked improvement in appearance, but not completely optimal, reduction of lesions by ≥ 50% and <100%).
3	Slight partial response	Improved or somewhat better patient (appearance slightly better than initial condition, but needs more treatments, <50% lesions decrease).
4	Non-response	No change (the same number and size of lesions as at the start of treatment).
5	Progression	Worse (increased number or size of lesions).

**Adverse events**

Adverse events reported in the reviewed literature are pain, edema, and ecchymosis at the microinjection site [1,2].

**Classification of adverse events (Table 5)[7]**

**Degree of satisfaction of patients to treatment**

The degree of satisfaction (PSSS) of the patients with the treatment was evaluated taking into account what was reported

by the patient according to the scale (Table 6) [8].

**Bioethical considerations**

The protocol was submitted to the consideration and approval of a Review and Ethics Committee for Clinical Research created for this purpose, which evaluated it from an ethical point of view. Additionally, this protocol was submitted to scientific and methodological review and approval by the Institutional Scientific Council of the Hospital Clínico Quirúrgico “Hermanos Ameijeiras”.

**Table 5:** Intensity scale of adverse events [7].

Intensity	Characteristics
Mild	if the adverse event subsided without treatment.
Moderate	if treatment was required, but the adverse event subsided with it.
Serious	if he required hospitalization or did not yield to treatment.
Very serious	if it endangered the life of the patient, if it caused sequelae or disability.

**Table 6:** Scale of the degree of patient satisfaction [8].

Evaluation		Degree of satisfaction
1	Very bad	I did not get any improvement and the treatment caused me multiple discomforts (inflammation, bruising and pain).
2	Bad	I did not get any improvement, but the treatment did not cause me any discomfort.
3	Regular	The improvement was little.
4	Good	The improvement was noticeable, but not total.
5	Very good	The improvement was complete with minimal discomfort.

**Statistical methods used**

The medical records of the patients included in the study were stored in the Department’s file. With the information gathered, a Microsoft Office version XP database in Excel format was created, which was exported to the SPSS version 21.0 system for analysis. To summarize the information of the study sample, the arithmetic mean, standard deviation and minimum and maximum values will be used. The Student’s t test was used for all quantitative variables. For all qualitative variables (degree of aesthetic improvement, degree of affectation of the volume of the hand and degree of satisfaction), the absolute numbers and percentages were calculated before and after the treatment, which were compared using Pearson’s Chi-square test. In all the hypothesis tests carried out, a significance level  $\alpha = 0.05$  was performed.

**Sample’s size calculation**

The sample size was calculated using the C4-Study Design Pack computerized program. (C4- SDP) for sample size calculation

(CTM). Version 1.1 © Glaxo Wellcome. SA; [9] considering the following values: percentage of success reported in the literature 70%, percentage of success in the current study of 80%. With an alpha error of 0.05, a power of 80% and covering a loss of 5% of the patients, it was necessary to have 60 subjects in total.

**Results**

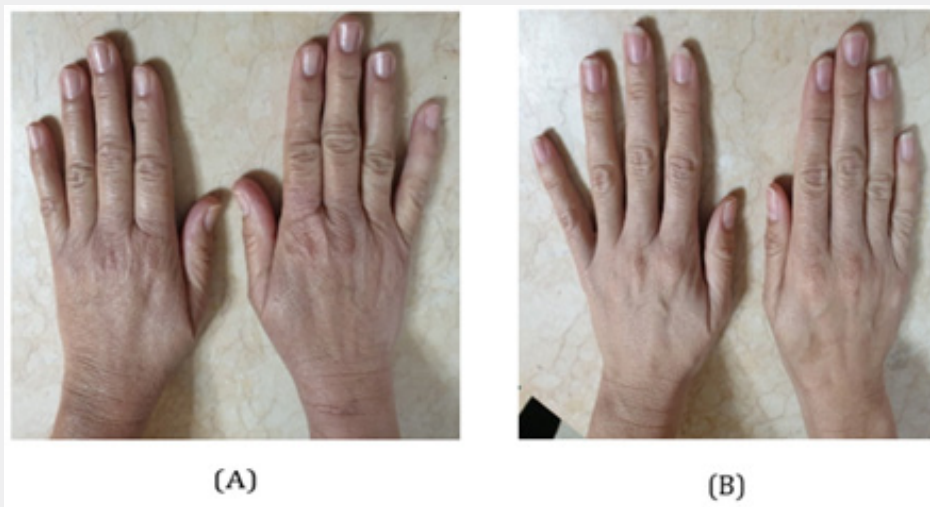
The study sample consisted of 60 women with skin phototypes between II and IV. The average age ranged around  $45 \pm 4.3$  years (Table 7). Regarding the Glogau Photodamage Scale, 51 patients were classified as grade III, and 9 as grade II before the start of the study. After treatment, 33/51 (64.7%) patients who were classified as grade III were reclassified as grade II and 6/9 (66.6%) patients who were classified as grade II were reclassified as grade I ( $p = 0.012$ ); the rest of the patients remained in the same grade assigned before treatment. According to the Global Esthetic Improvement Scale, there were significant changes after treatment ( $p < 0.001$ ); 3/60 (5%) patients achieved a total response, 37/60 (61.6%) patients achieved a marked partial response, and 20/60

(33.3%) patients achieved a slight partial response (Figure 1 & 2). Regarding the Scale of the degree of involvement of the volume of

the hand, 51 patients were classified as grade III, 6 as grade II and 3 as grade I before the start of the study.



**Figure 1:** Images showing the improvement of the skin on the back of the hands of a patient (A) before and (B) three months after treatment with APC.



**Figure 2:** Images showing the improvement of the skin on the back of the hands of another patient (A) before and (B) three months after treatment with APC.

**Table 7:** Epidemiological and clinical characteristics of the subjects.

	Mean (SD)	45.6 (±4.3)	
	(Minimum; Maximum)	(27; 58)	
Age		N	%
	20-29	15	25
	30-39	12	20
	40-49	27	45
	50-60	6	10
Sex	Female	60	100

Skin phototype	II	24	40,0
	III	33	55
	IV	3	5
Glogau	II	9	15
	III	51	85
HVRS	Si1 1	3	5
	2	6	10
	E 3	51	85

**Table 8:** Adverse events.

		APC N=60	
		N	%
Adverse events	Pain	60	100
	Inflammation	50	83.3
	Equimosis	10	16.7
Duration	Less than 7 Days	60	100
intensity	Light	60	100
Attitude	No Changes	60	100
Result	Resolved	60	100

**Table 9:** Degree of satisfaction, according to the patients' own satisfaction scale (PSSS).

Satisfaction	APC N=60		P
	N	%	
Regular	0	0	<0.001 (x <sup>2</sup> )
Good	16	26.6	
Very Good	44	73.4	

After treatment, 35/51 (68.6%) patients who were classified as grade III were reclassified as grade II, 4/6 (66.6%) patients who were classified as grade II were reclassified as grade I and 2 / 3 (66.6%) patients who were classified as grade I were reclassified as grade 0 (p = 0.018); the rest of the patients remained in the same grade assigned before treatment. All the patients reported some adverse event (pain, inflammation and ecchymosis), which were of slight intensity, did not imply changes before the intervention and were completely resolved. The pain occurred during the procedure and disappeared immediately after the completion of the procedure (100%), the inflammation (83.3%) lasted 2 to 3 days and the ecchymosis at the puncture sites (16.7%) were infrequent and of short duration (five to seven days in duration) (Table 8). Of the 60 patients treated with APC, 16/60 patients (26.6%) reported a good degree of satisfaction and a very good degree of satisfaction 44/60 patients (73.4%), because they achieved evident improvement with respect to their condition initial (Table 9).

## Discussion

Platelets play a vital role in initiating hemostasis and wound healing. In response to tissue and vascular damage, a platelet plug is formed, with the subsequent release from its alpha granules of more than 30 biologically active proteins, including: transforming growth factor  $\beta$ , platelet-derived factor, growth factor, vascular endothelial growth factor, fibroblast growth factor, and epithelial cell growth factor. These factors not only aid in clotting but also drive angiogenesis and promote tissue repair and regeneration [10]. Multiple authors have shown that topical application or intradermal injection of PRP and its growth factors produce favorable cutaneous changes: clinical (restores its vitality, increases its thickness, recovers its elastic consistency, improves blood circulation, increases its smoothness, decreases its wrinkles and improves their appearance) [2,10,11] histopathological (increases the number of fibroblasts, collagen fibers and blood vessel basement membranes) [2,10,12] immunohistochemical (improves collagen expression type I, III and IV) [13-15] and the genetic material (through the polymerase chain reaction expression of three target genes, such as: collagen IA, matrix metalloproteinase gene 1 and protein rich in proline of keratinocytes) [13,14]. PRP has been used as an adjunct to multiple skin rejuvenation treatments (lipotransference, laser, peeling, lifting).

In all the studies reviewed these treatments expected a higher response when combined than alone [12,16-18], PRP has also been used to reduce the intensity and duration of adverse events in these modalities. In a study by Kim H. and Gallo J, they were able to objectively reduce erythema and edema after treatment with fractional carbon dioxide laser by administering intradermal PRP (P = 0.02), associated with fewer subjective symptoms reported by patients (itching, burning and pain) [18]. There is only one previous report on the use of PRP as a rejuvenating monotherapy of the back of the hands, which was carried out by Cabrera-Ramírez JO and collaborators who applied 3 sessions of subcutaneous PRP with a cannula on the back of the hands. At the end of the treatment, the subjects had clinical improvement in the Fitzpatrick wrinkle and elastosis classification scale (p <0.001) and in the Glogau photodamage scale (p = 0.01) and a histological increase in the number of fibroblasts (p = 0.000), number of vessels (p = 0.000) and amount of collagen (p = 0.27) [2]. In our study there was clinical improvement in the Glogau photodamage scale (p = 0.012), in the global scale of aesthetic improvement (p = 0.001)

and in the scale of the degree of involvement of the volume of the hand ( $p = 0.018$ ).

## Conclusion

The application of autologous platelet concentrate proved to be effective and safe in reducing the signs of skin aging on the back of the hands, associated with a high degree of patient satisfaction.

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