Research Article

Dermatology Research

Efficacy and Safety of Autologous Platelets Concentrate in the Treatment of Crow's Feet Photo Aging

Israel Alfonso Trujillo*, Yetter Cruz Leon, Mariana Sarao Pineda, Nora Rosales Hernández, Yaquelin Luciana Morales Novo, Jesus Lazaro Diego De la Campa, Angel, Rosa Gutierrez Rojas, Julio Antonio López Silva and Daymi Serpa Almaguer

Clinical Surgical Hospital, Hermanos Ameijeiras, Havana Cuba.

***Correspondence:**

Israel Alfonso-Trujillo, Calzada de Managua # 1133 between Cayman and Quemados, Las Guásimas, Arroyo Naranjo, Havana, Cuba, CP: 19320.

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ABSTRACT

Introduction: *Platelet rich plasma (PRP) is an autologous serum that contains high concentrations of platelets and growth factors. It is currently a versatile therapy in dermatology; however, few studies objectively evaluate its efficacy.*

Objective: *To evaluate the efficacy and safety of intradermal microinjection of autologous platelet concentrate (APC) in the treatment of crow's feet rejuvenation.*

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: *60 women with an average age of 45 ± 4.3 years were treated. After treatment, there were significant changes in the Glogau Photo Damage Scale (P = 0.0022), in the Photonumeric Scale to assess the severity of crow's feet (P = 0.0111) and in the Global Aesthetic Improvement Scale. (P = 0.0033). The adverse events found were pain, inflammation and ecchymosis. The degree of satisfaction reported by the patients was good (16.6%) and very good (83.3%) (P = 0.0021).*

Conclusions: *The autologous platelet concentrate proved to be effective and safe in reducing the signs of cutaneous aging of crow's feet, associated with a high degree of patient satisfaction.*

Keywords

Platelet-rich plasma, Crow's feet rejuvenation, Cutaneous photoaging of crow's feet, Autologous platelet concentrate.

Introduction

Platelet Rich Plasma (PRP) is an autologous serum that contains high concentrations of platelets and growth factors. These growth factors are responsible for the mitogenesis and differentiation of monocytes, fibroblasts, stem cells, keratinocytes and endothelial cells, as well as inducing cell proliferation, angiogenesis and chemotaxis, in addition to containing serotonin, dopamine, histamine, adenosine and calcium, which increase the permeability of the membrane [1,2]. These qualities have made PRP a versatile therapy in dermatology; however, few studies objectively

evaluate its efficacy, which motivated the conduct of the present investigation.

Goals

The primary objective was to determine the efficacy and safety of autologous platelet concentrate (APC) microinjection in the treatment of crow's feet photoaging and the secondary objectives were: 1) to evaluate the clinical response to treatment, 2) to evaluate type e 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 CPA was applied monthly for 12 months. Three months after the end of the treatment, the response to it was evaluated (final evaluation), comparing the current state with the initial state; for this, and the patient had to attend the scheduled consultation. Throughout the study, there was a rigorous control of adverse reactions. Before and after the procedure, the platelets were quantified to determine the quality of the applied product (the average degree of concentration of the platelets after the procedure increased 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 to IV according to Glogau's classification, [3] grade 1 to 4 according to the photonumeric scale for the evaluation of the severity of crow's feet, [4] normal complementary tests (hemogram with differential, coagulogram, blood chemistry and serology for HIV, hepatitis B and C), with signed informed consent.

Exclusion criteria (Table 1).

Table 1: 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.

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 subject's 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 blood was performed total 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 of PRP were obtained; 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 among the crow's feet, forehead, other facial areas, V of the neckline, neck and back of the hands. Asepsis and antisepsis of the back of the hands were performed. Subsequently, with a 27G × 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 2), [3] the photonumeric scale for the evaluation of the severity of crow's feet (Table 3) [4] and the global aesthetic improvement scale (GAIS) (Table 4) [6].

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].

Table 2: 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 3: Photonumeric scale for the evaluation of the severity of crow's feet [4].

Grade	Characteristics
0	Without wrinkles.
1	Very fine wrinkles, hardly noticeable.
2	Fine and superficial wrinkles.
3	Moderately deep wrinkles.
4	Deep wrinkles, with well-defined edges.

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).

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.

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 subjected to scientific and methodological review and approval by the Institutional Scientific Council of the Hospital Clínico Quirúrgico "Hermanos Ameijeiras".

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 were used. For all quantitative variables, the student's t test was used. For all qualitative variables (degree of photodamage, degree of aesthetic improvement, degree of severity of crow's feet and degree of satisfaction), the absolute numbers and percentages before and after treatment were calculated, which were compared using the Chi test. Pearson's square. In all hypothesis tests carried out, a significance level $\alpha = 0.05$ was used.

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 ± 4.3 years (Table 7).

Table 7: Epidemiological and clinical characteristics of the subjects.

	Mean (SD)	45.6 (±4.3)	
	(Minimum; Maximum)	(27; 58)	
		N	%
Age	**20-29**	15	25.0
	30-39	12	20.0
	40-49	27	45.0
	50-60	6	10.0
Sex	**Female**	60	100.0
Skin phototypes	**II**	24	40.0
	III	33	55.0
	IV	3	5.0
Glogau	**II**	9	15.0
	III	51	85.0
Degree of severity of crow's feet	**22 2**	10	16.6
	3	18	30.0
	E 4	32	53.3

Regarding the Glogau Photo Damage Scale, 51 patients were classified as grade III, and 9 as grade II before the start of the

study. After treatment, 28/51 (54.9%) patients who were classified as grade III were reclassified as grade II and 7/9 (77.7%) patients who were classified as grade II were reclassified as grade I (p = 0.0022); the rest of the patients remained in the same assigned grade before treatment.

Regarding the photo numeric scale to assess the severity of crow's feet, 32 patients were classified as grade IV, 18 as grade III, and 10 as grade II before the start of the study. After treatment, 18/32 (56.2%) patients who were classified as grade IV were reclassified as grade III, 16/18 (88.8%) patients who were classified as grade III were reclassified as grade II, and 9 / 10 (90.0%) patients who were classified as grade II were reclassified as grade I (p = 0.0111); the rest of the patients remained in the same assigned grade before treatment.

According to the Global Esthetic Improvement Scale, there were significant changes after treatment (p <0.0033); 5/60 (8.3%) patients achieved a total response, 40/60 (66.6%) patients achieved a marked partial response, and 15/60 (25.0%) patients achieved a slight partial response (Figures 1 and 2).

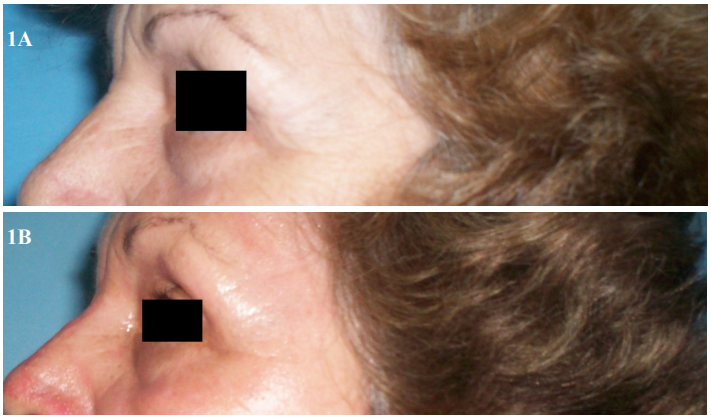

Figure 1: Images showing the improvement of the skin on the crow's feet of a patient (A) before and (B) three months after treatment with APC.

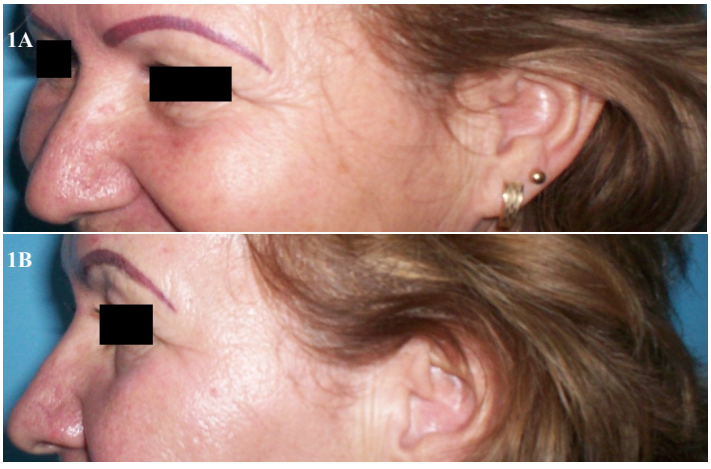

Figure 2: Images showing the improvement of the skin on the crow's feet of another patient (A) before and (B) three months after treatment with APC.

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 (33.3%) lasted 2 to 3 days and the ecchymoses at the puncture sites (6.6%) were infrequent and of short duration (five to seven days in duration) (Table 8).

Of the 60 patients treated with CPA, 10/60 patients (16.6%) reported a good degree of satisfaction and 50/60 patients (83.3%) reported a very good degree of satisfaction, because they achieved evident improvement with respect to their condition initial (Table 9).

Table 8: Adverse events.

		APC N = 60	
		N	%
Adverse events	Pain	60	100.0
	Inflammation	20	33.3
	Equimosis	4	6.6
Duration	Less than 7 days	60	100.0
intensity	Light	60	100.0
Attitude	No changes	60	100.0
Result	Resolved	60	100.0

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

Satisfaction	APC N = 60		p
	N	%	
Regular	0	0	<0,0021 (χ^2)
Good	10	16.6	
Very good	50	83.3	

Discussion

Although it is impossible to stop the passage of time, skin aging goes beyond aesthetics since it can greatly affect the quality of life of patients, so it is very important to know the different mechanisms that originate it and become familiar with the various anti-aging strategies that exist today. In addition, it is essential that the doctor understand the wishes and expectations of the patient in order to guide him towards a therapeutic modality that leads to the best results [10].

Yuksel EP et al conducted an investigation with the aim of evaluating the efficacy of PRP for facial skin rejuvenation. It included 10 patients who were injected with PRP in crow's feet every 15 days until completing 3 sessions. The evaluation of the response (scale from 0 to 5 of the severity of wrinkles, pigmentation and skin texture) was carried out by three dermatologists and by the patient himself before each procedure and 3 months after the last session. In the final evaluation, there was a significant improvement in the scale of severity of wrinkles, texture and pigmentation of the skin according to the evaluation of the patients; while only the improvement in skin texture was significant as assessed by dermatologists [11].

Cameli N et al with the aim of evaluating the efficacy and safety of dermal injections of autologous PRP in the rejuvenation of facial skin carried out a study that included 12 patients who underwent three treatment sessions at intervals of one month. The results were evaluated from the clinical and instrumental point of view (transepidermal water loss, corneometry, cutometer, visioscan and visioface) before and one month after finishing the treatment. The results showed significant improvement in skin texture, smoothness, barrier function, and capacitance ($p < 0.05$) [12].

Kang BK et al published a study in which they included 20 Asian women (mean age 50.6 ± 3.7 years; range 44-57 years) with the objective of determining the efficacy and safety of PRP in periocular rejuvenation. Ten patients received PRP on one side of the face and platelet-poor plasma (PPP) on the other side of the face. Ten patients received PRP on one side of the face and saline solution (SS) on the other side of the face. Subjects underwent three treatment sessions by injections at 4 weeks intervals. The evaluations of the results were carried out 3 months after the final treatment; included a self-assessment using a questionnaire, subjective satisfaction scale, and clinical evaluation performed by three blinded dermatologists who compared photographs obtained at the beginning of the study and at the last follow-up. Erythema and melanin indices were also evaluated by spectrophotometry. The results of the 3-month follow-up visit showed that PRP-treated skin achieved significant improvement in wrinkles and skin tone compared to PPP or SS-treated skin ($P < 0.05$). Also, in the skin treated with PRP, the erythema index decreased from 8.52 to 7.37 ($P = 0.01$) and melanin from 34.42 to 31.86 ($P < 0.01$). Adverse events were pain in 4/20, erythema in 10/20, edema in 5/20, and purpura in 6/20 patients; All of mild intensity and spontaneous resolution [13].

Karabudak AO et al. conducted a prospective, single-center, controlled and non-randomized study in 20 women aged between 40 and 49 years with the objective of measuring the mean optical density (MOD) of collagen in the facial area treated with PRP. PRP was injected in the right infra-atrial area and the whole face and saline solution (SS) only in the left infra-atrial area (control). Histopathological examinations were performed before and 28 days after treatment. The results showed that the collagen MOD of the facial area treated with PRP reached an improvement of 89.05% when compared to the pre-treatment MOD. The ratio of improvement from PRP to SS (89.05% to 46.01%) was 1.93: 1 ($p < 0.001$). No serious side effects were detected [14].

In our study, there was clinical improvement in the Glogau photodamage scale ($P = 0.0022$), in the photo numeric scale to assess the severity of crow's feet ($P = 0.0111$) and in the global scale of aesthetic improvement ($P = 0.0033$), associated with a high degree of patient satisfaction ($P = 0.0021$).

Conclusions

The application of autologous platelet concentrate proved to be effective and safe in reducing the signs of cutaneous aging of crow's feet, associated with a high degree of patient satisfaction.

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