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Research Article

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Efficacy and Safety of Autologous Platelet Concentrate in The Treatment of aging of The Neck.

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Abstract

Introduction: *Neck rejuvenation has a certain degree of difficulty, both due to its location and mobility, as well as its anatomical characteristics.*

Objective: *To evaluate the efficacy and safety of intradermal microinjection of autologous platelet concentrate (APC) in the treatment of signs of neck aging.*

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 = = 0.024), in the Global Aesthetic Improvement Scale (P <0.002) and in the Allergan Neck Transverse Lines Scale (P = 0.013). The adverse events found were pain, inflammation and ecchymosis. The degree of satisfaction reported by the patients was good (10.0%) and very good (90.0%) (P < 0.0012).*

Conclusions: *The autologous platelet concentrate proved to be effective and safe to reduce the signs of aging in the neck, associated with a high degree of patient satisfaction.*

Key Words: Platelet Rich Plasma. Neck Rejuvenation. Skin Photoaging. Autologous Platelet Concentrate. Aging of the neck.

Introduction

Neck skin is often especially vulnerable to photodamage because it is one of the anatomical regions most exposed to ultraviolet radiation. Sometimes their appearance tends to offer better information than the face about the biological age of the patient. Neck rejuvenation has a certain degree of difficulty, both due to its location and mobility, as well as its anatomical characteristics. At present, the use of less invasive aesthetic medical procedures based on the application of platelet-rich plasma (PRP) and its growth factors (FC) have reached great popularity [1, 2]. however, few studies objectively evaluate their effectiveness, which motivated 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 the signs of aging of the neck 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 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 of the lesions (wrinkles, lines and transverse grooves of the neck, pigmentation, senile lentigo, actinic keratosis) 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 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, III (Glogau classification), grades 1 to 4 of the Allergan neck transverse line scale(4), normal complementary tests (hemogram with differential, coagulogram, blood chemistry and serology for HIV, hepatitis B and C), with signed informed consent [3].

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.

Treatment

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 (CRD). The blood was extracted (500 milliliters), then the CPA was obtained with the Rotixa centrifuge (221 mm radius) according to international standards [5]. To obtain the CPA, a first light centrifugation of the whole blood was carried out in the plastic bag for 3 minutes at 2800 rpm at 22 oC, 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 with PRP in the plastic bag for 5 minutes at 4500 rpm at 22 oC, 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 re-

turned to the patients and finally a microinjection of 10 milliliters of the CPA was performed, distributed among the neck, the facial area, the back of the hands and the V of the neckline.

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 classification scale) (Table 2) [3], the scale of transverse lines of the Allergan neck (Table 4) [4] and the global aesthetic improvement scale (GAIS) (Table 3) [6].

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: Escala de líneas transversales del cuello de Allergan [4].

Grade		Characteristics
0	None	No transverse neck lines.
1	Minimal	Minimal superficial transverse lines of the neck.
2	Moderate	Moderate transverse lines, erasable with neck extension movements.
3	Severe	Deep transverse lines, not erasable with neck extension movements.
4	Extreme	Non-erasable deep transverse neck grooves, with redundant skin.

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].

Table 5: Intensity scale of adverse events

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.

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 6. Scale of the degree of patient satisfaction

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 (PRE) 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 (CCI) 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 prepared, 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 photoaging, degree of aesthetic improvement, degree of neck involvement and degree of satisfaction), absolute numbers and percentages before and after treatment were calculated, which were compared using Pearson's Chi-square test. 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 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 6).

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, 30/51 (58.8%) patients who were classified as grade III were reclassified as grade II and 5/9 (55.5%) patients who were classified as grade II were reclassified as grade I ($p = 0.024$); the rest of the patients remained in the same grade assigned before treatment.

According to the Global Aesthetic Improvement Scale, there were significant changes after treatment ($p < 0.002$); 8/60 (13.3%) patients achieved a total response, 30/60 (50.0%) patients achieved a marked partial response, and 22/60 (36.7%) patients achieved a slight partial response. Regarding the Allergan Neck Transverse Lines Scale, 32 patients were classified as grade 5, 14 as grade 4, 7 as grade 3, 4 as grade 2 and 3 as grade 1, before the start of the study. After treatment, 23/32 (71.8%) patients who were classified as grade 5 were reclassified as grade 4, 9/14 (64.2%) patients who were classified as grade 4 were reclassified as grade 3, 5 / 7 (71.4%) patients who were classified as grade 3 were reclassified as grade 2, 3/4 (75%) patients who were classified as grade 2 were reclassified as grade 1 and 3/3 (100%) patients who were classified as grade I were reclassified as grade 0 ($p = 0.013$); the rest of the patients remained in the same grade assigned before treatment (Figure 1 and 2).

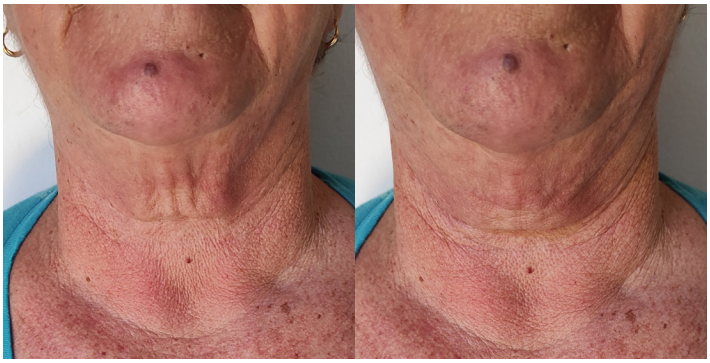

Figure 1: Images showing the changes in the Allergan Neck Transverse Lines Scale (1A) before and after (1B) treatment with CPA

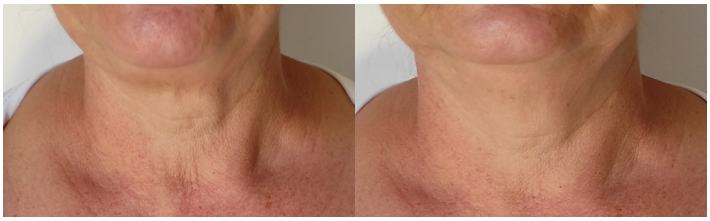

Figure 2: Images showing the changes in the Allergan Neck Transverse Lines Scale (2A) before and after (2B) treatment with CPA.

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 (10%) lasted 2 to 3 days and the ecchymoses at the puncture sites (5%) they were infrequent and of short duration (five to seven days in duration) (Table 7).

Table 7: Epidemiological and clinical characteristics of the subjects.

Age	**Mean (SD)**	**45.6 (±4.3)**	
	(Minimum; Maximum)	**(27; 58)**	
		N	**%**
	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 phototype	II	24	40.0
	III	33	55.0
	IV	3	5.0
Glogau	II	9	15.0
	III	51	85.0
Degree of transverse lines	22 1	3	5.0
	2 2	4	6.6
	3	7	11.6
	4	14	23.3
	E 5	32	53.3

Of the 60 patients treated with CPA, 6/60 patients (10.0%) reported a good degree of satisfaction and 54/60 patients (90.0%) reported a very good degree of satisfaction, due to the fact that they achieved evident improvement with respect to their condition initial (Table 8).

Table 8. Adverse events

		APC N = 60	
		N	%
Adverse events	PAIN	60	100.0
	INFLAMMATION	6	10.0
	EQUIMOSIS	3	5.0
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	<0,0012 (χ^2)
GOOD	6	10,0	
VERY GOOD	54	90,3	

Discussion

In recent years, platelet-rich plasma, collagen peptides, and stem cells have become popular treatments for skin rejuvenation. Massive consumer promotion through the Internet and social media has drawn the attention of the beauty industry to these treatments. The reviewed studies affirm the effectiveness of this new therapeutic trend in the world of aesthetic medicine.

Redaelli A et al. Conducted a study in 23 patients with the objective of evaluating real results, benefits and side effects of PRP in revitalizing aging skin. The patients were treated with a monthly session of injections with 4 ml of PRP (a total of three sessions). The study was imaged before and after each session using a dermatoscope, a digital camera, a state-of-the-art comprehensive imaging system, and imaging software. Results were evaluated one month after the last session by photographic score, patient satisfaction score, and physician satisfaction score. Finally, a final graded score was calculated for each patient. In general, the results were satisfactory. No serious and persistent side effects were detected [10].

Abuaf OK et al. Enrolled a non-randomized, open-label, prospective controlled clinical trial conducted in 20 women aged between 40 and 49 years, who were injected with saline solution in the left infra-atrial area (control) and PRP in the infra-atrial area right and all over the face. Histopathological examinations were performed before and 28 days after treatment. The mean optical densities (MOD) of collagen were measured in the pretreatment, control and PRP treated area. The MOD in the PRP-treated group showed an 89.05% improvement when compared to the pre-treatment MOD. The MOD in the control group showed improvement of 46.01% when compared to the pre-treatment MOD. The MOD of the collagen fibers was clearly higher on the PRP side than in the control group ($p < 0.001$). No serious side effects were detected [11].

Everts PA et al. To evaluate the efficacy of autologous injections of neutrophil-poor PRP in skin rejuvenation administered 3 treatment sections to 11 patients. The efficacy of the procedures was evaluated using biometric parameters (subepidermal low echogenicity band = SLEB) and a self-assessment questionnaire of the patient's outcome at each visit and at 6-month follow-up. A significant decrease in the number and size of brown spots ($P < 0.05$) was observed after 3 months. The number and depth of wrinkles were significantly reduced ($P < 0.05$). A decrease in the thickness of SLEB was observed 2 months after the first injection, with an increase in the density of SLEB ($P < 0.05$ for both parameters), without affecting the thickness of the subcutaneous fat. Self-assessment at 6-month follow-up revealed a mean satisfaction score of> 90% [12].

Maisel-Campbell AL et al. Conducted a systematic review looking for prospective trials and case series with 10 patients or more, from the start of PRP use until March 2019, to evaluate the evidence on its safety and effectiveness in reducing visible signs of aging. Twenty-four studies were included, including eight randomized controlled trials, representing a total of 480 patients. According to the global evaluation of the doctors, it was shown that inject-

able therapy induces an improvement in the appearance, texture, pigmentation and fine lines of the skin, with adequate safety and a high degree of patient satisfaction. They found heterogeneity in the preparation and administration of the PRP and the lack of standardization in the outcome measures as a limitation. They recommended conducting more high-quality trials with sufficient follow-up to optimize treatment regimens [13].

In our study, 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 = 0.024), in the Global Esthetic Improvement Scale (P <0.002) and in the Allergan Neck Transverse Lines Scale (P = 0.013). The adverse events found were pain, inflammation and ecchymosis. The degree of satisfaction reported by the patients was good (10.0%) and very good (90.0%) (P <0.0012), so it is concluded that autologous platelet concentrate is effective and safe to reduce signs of neck aging, associated with a high degree of patient satisfaction.

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