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Peeling with 25% Trichloroacetic Acid Associated with 30% Salicylic Acid in the Treatment of Facial Skin Photo aging

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ABSTRACT

Introduction: *Despite the growing therapeutic options for skin rejuvenation, superficial chemical peels have proliferated both in popularity and in product diversity. These qualities have made the peel an indispensable tool in the therapeutic arsenal of dermatology, however, few studies objectively evaluate its effectiveness.*

Objective: *To evaluate the efficacy and safety of peeling with 25% trichloroacetic acid associated with 30% salicylic acid in the treatment of facial skin rejuvenation.*

Method: *An observational, analytical and longitudinal study was carried out in 220 patients from two hospitals (Surgical Clinic: "Hermanos Ameijeiras" and General Teaching: "Enrique Cabrera"), in the period between January 2010 and January 2020. Treatment It was applied monthly for 6 months. The final evaluation was carried out 3 months after the end of the treatment.*

Results: *192 women and 28 men were treated with an average age of 38.4 (± 5.8) years. After treatment, there were significant changes in the Glogau Photo Damage Scale (P = 0.001), in the Lemperle Wrinkle Assessment Scale (P = 0.009) and in the Global Aesthetic Improvement Scale (P = 0.016). The adverse events found were burning, inflammation and scaling. The degree of satisfaction reported by the patients was good (3.7%) and very good (86.3%) (P = 0.003).*

Conclusions: *The 25% trichloroacetic acid peel associated with 30% salicylic acid proved to be effective and safe to reduce the signs of facial skin aging, associated with a high degree of patient satisfaction.*

Keywords: *Chemical peeling. Rejuvenation of facial wrinkles. Facial skin photoaging. Salicylic acid. Trichloroacetic acid.*

INTRODUCTION

Modern medicine has increased both the average life expectancy and the quality of life in the general population. Due to this development, there has been an increased demand for the treatment of age-related skin changes. Despite the growing therapeutic options for skin rejuvenation, superficial chemical peels have proliferated both in popularity and in product diversity.[1,2] These qualities have made the peel an indispensable tool in the therapeutic arsenal of 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 peeling with 25% trichloroacetic acid associated with 30% salicylic acid in the treatment of facial skin photo aging, 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 380 patients from two hospitals (Surgical Clinic: "Hermanos Ameijeiras" and General Teaching: "Enrique Cabrera"), in the period between January 2010 and January 2020. Treatment with 25% trichloroacetic acid associated with 30% salicylic acid was applied monthly for 6 months. Three months after the end of the treatment, the response to it was sent

(final evaluation), comparing the current state 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.

Inclusion Criteria

Patients between 20 and 60 years of age, of any sex, skin photo type I to III according to Fitzpatrick's classification,[3] skin photo aging grade II to IV according to Glogau's classification,[4] grade 1 to 4 according to the scale of evaluation of the Lemperle's wrinkles,[5] normal complementary tests (hemogram with differential, coagulogram, blood chemistry and serology for HIV, hepatitis B and C), with signed informed consent.

Table 1. *Exclusion criteria and their relationship with the time limits to perform the procedure.*

Criteria	Time limits
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.
Herpes simplex infection and / or other septic foci.	Simultaneous to the procedure.
Prone to forming keloids.	Before the procedure.
Application of topical retinoids, aesthetic treatments in the region to be treated, including lasers, intense pulsed light, chemical peels, mesotherapy, carboxytherapy, face lift or others.	Three months prior to the procedure.
Fillers in the region to be treated.	One year prior to the procedure.
Hormonal treatment (estrogens, progesterone, hormonal contraceptives, etc.).	One year prior to the procedure.
Ionizing radiation treatments.	Five years prior to the procedure.
Inadequate photoprotection.	Unlimited

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. One week before the intervention, it was indicated to apply tretinoin (gel) at night. The next technique for performing the peeling was: patient adaptation (inclined between 45 and 60 degrees); antiseptic cleaning and degreasing of the entire facial area with alcohol so that its penetration is homogeneous; Small cotton-tipped applicators were used to remove the solution and apply it to the skin; the patient's eyes remained closed throughout the procedure; abrasion sequentially from a forehead to the temples, then to the cheeks, and finally to the lips and eyelids. First, a single coat of the 25% trichloroacetic acid solution was applied evenly to achieve a white frost. Once the frost had formed, a single layer of the 30% salicylic acid solution was applied evenly. The eyelids were treated with delicacy and care. After an appropriate time, the solution can be diluted (not necessary, only if a yellowish-gray color appears in some area). If severe erythema appears, apply topical antibiotic ointment or mild topical corticosteroid cream. Finally, indications are made to patients about outpatient care and sun protection.

VARIABLES RELATED TO THE RESPONSE TO TREATMENT

The response to treatment was evaluated taking into account the patient examination of the patient, using the Glogau photodamage scale (Table 2),[4] the Lemperle wrinkle evaluation scale (Table 3)[5] and the scale of global aesthetic improvement (GAIS) (Table 4).[6]

Table 2. *Classification of photoaging according to Glogau.*[4]

Group I (mild)	Group II (moderate)	Group III (advanced)	Group IV (severe)
28-35 years old	35-50 years old	50-65 years old	60-70 years old

No keratoses	Early actinic keratoses: slight yellow skin discoloration	Actinic keratoses: obvious yellow skin discoloration with telangiectasias	Actinic keratoses and skin cancers
Little wrinkling	Early wrinkling: parallel skin lines	Wrinkling present at rest	Wrinkling: much cutis laxa of actinic, gravitational, and dynamic origin
No scarring	Mild scarring	Moderate acne scarring	Severe acne scarring
Little or no makeup	Little makeup	Wears makeup always	Wears heavy layers of makeup

Table3. *Lemperle wrinkle evaluation scale*[(5)]

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.
5	Very deep wrinkles, redundant crease.

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

The adverse events reported in the reviewed literature are burning, pain, edema, infections, hyper pigmentation and healing disorders (delayed healing or hypertrophic scar) at the site of application.[(7,8)]

Classification of adverse events (Table 5)[(9)]

Table 5. *Intensity scale of adverse events.*[(9)]

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).[(10)]

Table 6. *Scale of the degree of patient satisfaction.*[(10)]

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 for 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. Furthermore, this protocol was submitted 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. With the information collected, a Microsoft Office version XP database in Excel format was made, 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 tudent's t test was used for all quantitative variables. For all qualitative variables (degree of photodamage, degree of aesthetic improvement, degree of severity of wrinkles and degree of satisfaction), the absolute numbers and percentages before and after treatment were calculated, which were compared using the Chi-square test of Pearson. 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;[11] 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 220 subjects in total.

Results

The study sample consisted of 192 women and 28 men, with skin phototypes between II and IV. The average age ranged around 38.4 (± 5.8) years (Table 7).

Table7. *Epidemiological and clinical characteristics of the subjects.*

Age	**Mean (SD)**	38,4(± 5,8)	
	(Minimum; Maximum)	(28; 60)	
		N	%
	20-29	26	11.8
	30-39	86	39.1
	40-49	92	41.8
	50-60	16	25.7
Sex	**Female**	192	7.3
	Male	28	12.7
Skin phototype	**I**	0	0
	II	182	82.7
	III	38	17.3
Glogau	**II**	48	21.8
	III	52	23.6
Degree of the wrinkles.	**22 1**	120	54.5
	2 2	0	0
	3	62	28.2
	E 4	100	45.4

Regarding the Glogau Photo Damage Scale, 120 patients were classified as grade IV, 52 as grade III, and 48 as grade II before the start of the study. After treatment, 74/120 (61.6%) patients who were classified as grade IV were reclassified as grade III, 37/52 (71.2%) patients who were classified as grade III were reclassified as grade II, and 46/48 (95.5%) patients who were classified as grade II were reclassified as grade I ($p = 0.001$); the rest of the patients remained in the same assigned grade before treatment.

Regarding the Lemperle wrinkle assessment scale, 58 patients were classified as grade IV, 100 as grade III, and 62 as grade II before the start of the study. After treatment, 44/58 (75.8%) patients who were classified as grade IV were reclassified as grade III, 88/100 (88.0%) patients who were classified as grade III were reclassified as grade II, and 55 / 62 (88.7%) patients who were classified as grade II were reclassified as grade I ($p = 0.009$); the rest of the patients remained in the same assigned grade before treatment.

According to the Global Aesthetic Improvement Scale, there were significant changes after treatment (p = 0.016); 20/220 (9.1%) patients achieved a total response, 142/220 (64.5%) patients achieved a marked partial response, and 58/220 (26.4%) patients achieved a mild partial response (Figure 1, 2).

1A **1B**

Figure 1. *Images showing the improvement of the skin on the right side of a patient's face (A) before and (B) three months after peeling treatment with 25% trichloroacetic acid associated with 30% salicylic acid.*

2A **2B**

Figure2. *Images showing the improvement of the skin on the left side of the face of the same patient (A) before and (B) three months after the peeling treatment with 25% trichloroacetic acid associated with 30% salicylic acid.*

All patients reported some adverse event (burning, inflammation, desquamation), which were of slight intensity, did not imply changes before the intervention and were completely resolved. The burning occurred during the procedure and disappeared immediately after the completion of the procedure (100%), the inflammation (96.3%) lasted 2 to 3 days and the desquamation (100%) lasted 5 to 7 days of duration (Table 8).

Table 8. *Adverse events.*

		N = 220	
		N	%
Adverse events	**BURNING**	220	100.0
	INFLAMMATION	212	96.3
	DESQUAMATE	220	100.0
	HYPERPIGMENTATION	220	100.0

Of the 220 patients treated with a 25% trichloroacetic acid peel associated with 30% salicylic acid, 8/220 patients (3.7%) reported a good degree of satisfaction and a very good degree of satisfaction 212/220 patients (96.3%), because they achieved evident improvement with respect to their initial condition (Table 9).

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

SATISFACTION	N = 220		
	N	%	p
REGULAR	0	0	0,003 (χ^2)
GOOD	8	3,7	
VERY GOOD	212	96,3	

DISCUSSION

Chemical peels are a popular, relatively inexpensive, and generally safe method for treating some skin disorders and for refreshing and rejuvenating the skin. Chemical peels are classified according to their depth of action into superficial, medium and deep peels. The depth of the peel correlates with clinical changes, and the greatest change is achieved with deep peels. However, depth is also associated with longer healing times and the potential for complications. A wide variety of peels are available using various topical agents and concentrations. Superficial peels, penetrating only the epidermis, can be used to enhance the treatment of a variety of conditions, including acne, melasma, dyschromias, photo damage, and actinic keratosis. Medium-depth peels, which penetrate to the papillary dermis, can be used for dyschromia, multiple solar keratoses, superficial scars, and pigmentary disorders. Deep peels, commenting on the reticular dermis, can be used for severe photoaging, deep wrinkles, or scars. Peels can be combined with other facial rejuvenation techniques in the office to optimize results and improve patient satisfaction and allow clinicians to tailor treatment to individual patient needs. Successful results are based on careful patient selection, as well as the appropriate use of specific exfoliating agents. Used correctly, chemical peels have the potential to meet an important therapeutic need in the arsenal of the dermatologist and plastic surgeon.[12]

Kubiak M et al designed a study with the objective of comparing the efficacy and tolerability of glycolic acid (GA) at 70% with trichloroacetic acid (TCA) at 15% for the treatment of photo aging. Twenty female patients affected by photo damage were treated with graded concentrations of GA at 70% and TCA at 15%. Each patient underwent 5 sessions of these peels, with an interval of 14 days between each session. Four clinical parameters of evaluation of the living skin surface were measured (hydration, elasticity, melanin and erythema). The records were made before each treatment and 3 months after the last application. The results significantly improved clinical and statistical in both groups of patients in terms of elasticity and hydration. GA increases skin hydration faster. The decrease in melanin content in the skin occurred significantly after the application of a series of GA treatments. The increased severity of the erythema showed statistical significance after treatment with TCA.[13]

Lawrence N et al compared the efficacy and safety of a medium-depth chemical peel with the standard regimen of topical fluorouracil in the treatment of generalized facial actinic keratoses (AKs). Fifteen patients with severe facial actinic damage and similar amounts of AK on both sides of the face were treated on the left side with a single application of Jessner's solution (JS) and 35% trichloroacetic acid (TCA) and on the right side with applications twice a day of 5% fluorouracil cream for 3 weeks. Assessments were made before treatment and 1, 6, and 12 months after treatment. Visible AKs were counted, skin biopsies were randomly performed, adverse effects were monitored, and

patients were asked about preference and perceived efficacy. The results showed that both treatments reduced the number of visible AKs by 75% and produced equivalent reductions in keratinocyte atypia, hyperkeratosis, parakeratosis, and inflammation, without significant alteration of pre-existing solar elastosis and telangiectasia. Except for erythema that lasted 3 months in one patient, no adverse side effects were seen with chemical peel. The majority of patients preferred exfoliation to fluorouracil due to the single application and lower morbidity. The authors concluded that JS-induced medium-depth exfoliation and 35% ACT is a useful alternative therapeutic option for generalized facial AK, particularly for patients with poor adherence, because it equals fluorouracil in efficacy and is superior in terms of the convenience of a single application with little associated morbidity.[14]

Kubiak M et al conducted a study with the objective of comparing the efficacy and tolerability of exfoliation with 35% trichloroacetic acid (TCA) (group I) versus the combination of glycolic acid (GA) at 70% and TCA at 15 % (group II) for the treatment of photo damaged facial skin. Twenty patients were included in each group with types II and III of the Glogau photo aging scale. Each patient underwent five sessions of these peels, with an interval of 14 days between each session. The following skin aging parameters were examined before the treatments, before each session and 3 months after the last application: hydration, elasticity, melanin index and erythema index (MPA-5; Courage-Khazaka, Germany); and depth and volume of wrinkles (PRIMOS; GFMesstechnik GmbH, Germany). The results showed that both exfoliation methods achieved a significant improvement in all skin parameters: elasticity, hydration, melanin index and erythema index, however the addition of GA at 70% before the application of the chemical peel with TCA 15% achieved improvement significantly greater than that induced by TCA 35% in photo aging parameters (increased elasticity and hydration of the skin; reduction of melanin index and erythema index) and the improvements perceived by the subject. The 35% TCA peel is more effective in reducing wrinkles, despite lower tolerability. Both medium-depth chemical peels, which include 15% TCA in combination with 70% GA and 35% TCA alone, have been shown to be useful for the removal of superficial or epidermal lesions and for improving the texture of photo damaged facial skin (skin photoaged Glogau grade II-III).[15]

Trichloroacetic acid (TCA) alone or in combination with other agents is the mainstay of medium-depth chemical peels. Indications for medium-depth chemical peels include both medical conditions, such as diffuse photodamage with contiguous actinic keratoses, and cosmetic conditions, such as aging face and solar lentiginosis. The medium depth chemical peel with TCA is relatively simple and is associated with a favorable benefit / risk ratio. However, the proper selection of patients, paying attention to medical and psychological factors, requires significant experience. The histological basis for the rejuvenating effects of TCA peels is well established, with a consistent correlation between depth and TCA concentration. The clinical effects of medium-depth chemical peels are generally rewarding for both the patient and the clinician.[16]

In our study, there was clinical improvement in the Glogau photodamage scale (P = 0.001), in the scale for evaluation of the severity of Lemperle's wrinkles (P = 0.009) and in the global scale of better aesthetics (P = 0.016), associated with a high degree of patient satisfaction (P = 0.003). Adverse events were mild and without any permanent consequences on the individual.

CONCLUSIONS

The application of the peel with 25% trichloroacetic acid associated with 30% salicylic acid proved to be effective and safe in reducing the signs of facial skin aging, associated with a high degree of patient satisfaction.

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