

## Fractional CO<sub>2</sub> Laser versus Glycolic Acid and Topical Tretinoin in the Treatment of Macular Amyloidosis: A Comparative Study

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### Abstract

**Background:** Macular amyloidosis (MA) is a variant of primary localized cutaneous amyloidosis. Several modalities were used to treat macular amyloidosis with variable results.

**Aim of Study:** To compare the efficacy of fractional CO<sub>2</sub> laser versus glycolic acid peeling with topical tretinoin application in treating macular amyloidosis.

**Patients and Methods:** Twenty five female patients with macular amyloidosis aged between 19-59 years were treated by 4 sessions of fractional CO<sub>2</sub> laser on the right side and Glycolic acid (20%) peeling and topical tretinoin 0.025% cream in between the sessions on the left side at 3-week intervals. Clinical improvement in terms of global improvement score was evaluated. Satisfaction grade was also assessed.

**Results:** Both areas showed significant increase in the global improvement scale without significant difference between both areas.

**Conclusion:** Both fractional CO<sub>2</sub> Laser and glycolic acid peeling with application of topical tretinoin in between the sessions are effective in the treatment of macular amyloidosis.

**Key Words:** Fractional CO<sub>2</sub> laser – Macular amyloidosis – Glycolic acid – Topical tretinoin.

### Introduction

**PRIMARY** localized cutaneous amyloidosis (PLCA) is a form of localized cutaneous amyloidosis without any systemic involvement. Hyperpigmented reticulated macular pattern appears in the skin [1] with a usually unsatisfactory treatment results [2].

Improvement of PLCA was mentioned to occur using laser as CO<sub>2</sub> laser [3] through transepidermal elimination of amyloid deposits [4].

Also retinoids induce apoptosis and stimulate macrophages, resulting in the removal of redundant extracellular material [5].

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Glycolic acid facilitates the breakdown of corneosome causing desquamation of the epidermal cells [6].

**Aim of work:** Compare the efficacy of fractional CO<sub>2</sub> laser and glycolic acid peeling with topical tretinoin application in treating macular amyloidosis.

### Patients and Methods

**Study design:** Prospective comparative clinical trial that included twenty-five female patients with cutaneous macular amyloidosis, attending the out-patient clinic at Kasr Al-Aini Hospital, Faculty of Medicine, Cairo University in the period between November 2015 and February 2017.

#### *Inclusion criteria:*

Any sex and age above 18 years not using any topical treatment for at least one month or systemic treatment for at least 3 months prior to presentation.

#### *Exclusion criteria:*

Pregnant or lactating females or history of hypertrophic scars and keloids.

*The lesion of each patient was divided into 2 areas:*

Area A (Right side): Treated by Fractional CO<sub>2</sub> laser.

• Area B (Left side): Treated by Glycolic acid peeling and topical tretinoin in between the sessions.

*Fractional CO<sub>2</sub> laser (DEKA Smartxide DOT):*

- Power 15 watt.
- Spacing 400µm.
- Dwell time 600µm.
- Stacking 2.

Chemical peeling procedure was done by the following technique:

- 1- Using 2x2 cm gauze pieces, the skin was cleansed with alcohol and then degreased with acetone.
- 2- Glycolic acid (GA) solution (20%) was properly applied with a cotton pad over the skin and left for 3-5 minutes.
- 3- The peel was then properly neutralized with sodium bicarbonate (10%) solution.
- 4- The patient was asked to apply on the area treated by GA peel, a topical tretinoin cream with 0.025% (Acretin 0.025%)® daily at night and wash it at the morning.

#### Photographic documentation:

Photography was performed using the same digital camera (Nikon Coolpix S2800, 20 mega pixel, made in china) set at a fixed distance from the patient's affected skin before each treatment, after the last session by 4 and 8 weeks.

#### Global improvement scale (0-4):

- 0=No change.
- 1=1-25% improvement.
- 2=26-50% improvement.
- 3=51-75% improvement.
- 4=76-100% improvement.

#### Patient satisfaction:

- 0 Indicates no satisfaction.
- 1 Indicates mild satisfaction (<25%).
- 2 Indicates moderate satisfaction (25-50%).
- 3 Indicates very good satisfaction (51-75%).
- 4 Indicates excellent satisfaction (>75%).

#### Statistical methods:

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 24. Data was summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. For comparison of paired measurements within each patient the non-parametric Friedman test and Wilcoxon signed rank test were used. *p*-values less than 0.05 were considered as statistically significant. Correlations between quantitative variables were done using Spearman correlation coefficient,  $r_s$ . For comparing categorical data, Chi square ( $\chi^2$ ) test was performed. Exact test was used instead when the expected frequency is less than 5.

## Results

The study involved 25 patients with localized cutaneous macular amyloidosis. The mean age of the studied group was  $32.60 \pm 12.63$  years, ranging from (19-59) years. The median duration of disease was 5 years (range: 1-15 years). All patients were females. 21 patients (84%) were Fitzpatrick skin type IV, while 4 patients (16%) were skin type III.

The most common site of lesion was the back (15 patients, 60%), followed by the upper arms (8 patients, 32%) and the upper chest (2 patients, 8%).

23 patients completed the 4 sessions and 2 patients only dropped out. While 4 patients did not show up for follow-up visit.

#### Global improvement scale:

The mean global improvement of MA after treatment (4 weeks after last session) was  $2.52 \pm 0.9$  on the Right (laser) area and increased to  $2.82 \pm 0.81$  at follow-up visit (8 weeks after last session) and was  $2.61 \pm 0.78$  on the Left (peeling) area and increased to  $2.76 \pm 0.75$  at follow-up visit (8 weeks after last session) (Table 1).

Table (1) also shows that both areas of the lesions showed significant global improvement scales after treatment and follow-up visit ( $p < 0.001$ , for the 2 comparison areas) and there was no significant difference between both areas ( $p = 0.48$ ).

Table (1): Comparison between global improvement scales over time in the 2 areas.

	Global improvement scale		<i>p</i> -value
	Follow-up after 4 weeks	Follow-up after 8 weeks	
Right area	$2.52 \pm 0.9$	$2.82 \pm 0.81$	0.001
Left area	$2.61 \pm 0.78$	$2.76 \pm 0.75$	0.001
<i>p</i> -value	0.48	0.763	

It was noted that in patients with skin type III, there was better mean global improvement ( $3 \pm 0.82$ ) on the Right (laser) area than the Left (peeling) area ( $2.75 \pm 0.96$ ) and this improvement was also observed on follow-up visit. While in patients with skin type IV, there was better mean global improvement ( $2.58 \pm 0.77$ ) on the left area than the Right area ( $2.42 \pm 0.9$ ) (Table 2).

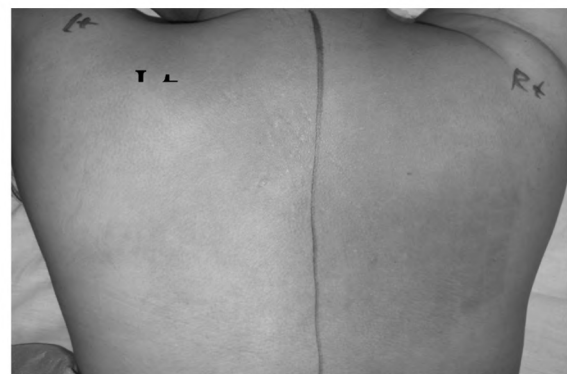
Table (2): Comparison between global improvement scale in Patients with skin type III and IV.

	Skin type III		Skin type IV	
	Rt area	Lt area	Rt area	Lt area
Follow-up after 4 weeks	$3 \pm 0.82$	$2.75 \pm 0.96$	$2.42 \pm 0.9$	$2.58 \pm 0.77$
Follow-up after 8 weeks	$2.75 \pm 0.5$	$2.5 \pm 0.58$	$2.85 \pm 0.9$	$2.85 \pm 0.8$

Treatment results showed that 9 patients (42.9%) had moderate satisfaction, 3 patients (14.3%) had very good satisfaction, 2 patients (9.5%) had excellent satisfaction and 7 patients (33.3%) had mild satisfaction on the right area. While on the left area, 8 patients (38.1%) had moderate satisfaction, 6 patients (28.6%) had very good satisfaction, 3 patients (14.3%) had excellent satisfaction while 4 patients (19%) had mild satisfaction.



(A)



(B)

Fig. (1): Clinical appearance of macular amyloidosis on the back of a patient. (A): Before treatment and (B): One month after the fourth session showing postinflammatory hyperpigmentation in the Rt area with and good clinical improvement in the Lt area.

## Discussion

In a study by Esmat et al., 2015 it was reported that fractional CO<sub>2</sub> laser provided measurable clinical and histological improvement and it was confirmed by the appearance of amyloid deposits in the epidermis suggesting their trans-epidermal elimination [7].

Besides increased elimination of amyloid material by laser, the fractional ablative effect of the laser could decrease the production of the amyloid material by correcting the process of keratinization

8.

Retinoids also can be used for improving cutaneous amyloidosis through its influence on keratin expression and thus inhibiting amyloid formation [9]. Moreover, inducing apoptosis stimulates macrophages to phagocytose amyloid deposits. These two effects may reduce the formation of amyloid [5].

Topical retinoids were used in some trials to improve cutaneous amyloidosis with variable results as in a case report that used topical tretinoin with a mild improvement in pruritus [10]. Nandini et al., 2014 conducted a study on 25 patients with MA using Trichloroacetic acid (TCA) (20%) peel

There was no significant difference in satisfaction between both areas ( $p=0.056$ ) (Table 3).

Table (3): Degree of patients' satisfaction after treatment (4 weeks after last session) in the whole studied group.

	Rt area	Lt area
Mild satisfaction	7 (33.3%)	4 (19%)
Moderate satisfaction	9 (42.9%)	8 (38.1%)
Very good satisfaction	3 (14.3%)	6 (28.6%)
Excellent satisfaction	2 (9.5%)	3 (14.3%)

and it concluded that TCA peel offers a good and cost-effective modality of treatment for patients with MA not responding to topical creams to give quite satisfactory results [11].

The current study proposed that application of Glycolic acid 20% would cause loosening of corneocyte adhesion facilitating the penetration of topical tretinoin deeper in the dermis to exert its effects. And there was a clinical improvement on both the treated areas.

It was noticed that in patients with skin type III, there was better mean global improvement in the laser treated area. While patients with skin type IV had better mean global improvement on the glycolic acid treated area. This could be due to the thermal effect of laser, which results in post-inflammatory hyperpigmentation in darker skin types.

## Declarations:

All authors confirm that there are no funding and no conflicts of interest.

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## ليزر ثاني أوكسيد الكربون التجزيئي مقارنة بالتقشير الكيميائي بحمض الجليكوليك مع التريتينوين الموضعي في علاج داء النشواني الجلدي البقعي : دراسة مقارنة

الخلفية: داء النشواني البقعي هو نوع من داء النشواني الجلدي الأساسي الموضعي. تم استخدام العديد من الطرق لعلاج الداء النشواني البقعي مع نتائج متغيرة.

هدف الموضوع: مقارنة فعالية ليزر ثاني أوكسيد الكربون الجزئي مقابل تقشير حمض الجليكوليك مع وضع تريتينوين دهان موضعي في علاج الداء النشواني البقعي.

طريقة العمل: تم علاج ٢٥ مريضة مصابات بالداء النشواني البقعي تتراوح أعمارهن بين ١٩-٥٩ سنة من خلال ٤ جلسات من ليزر ثاني أوكسيد الكربون الجزئي على الجانب الأيمن وتقشير حمض الجليكوليك (٢٠٪) وكريم تريتينوين الموضعي ٠.٠٢٥٪ بين الجلسات على الجانب الأيسر. تم تقييم التحسن السريري من حيث درجة التحسن العالمي. كما تم تقييم درجة الرضا.

النتائج: أظهر كلا المجالين زيادة كبيرة في مقياس التحسين العالمي دون اختلاف كبير بين المجالين.

الخلاصة: إن كلا من ليزر ثاني أوكسيد الكربون الجزئي وتقشير حمض الجليكوليك مع تطبيق تريتينوين الموضعي بين الجلسات فعال في علاج الداء النشواني البقعي.