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Fractional Carbon Dioxide Laser alone versus Fractional Carbon Dioxide Laser assisted Topical steroid delivery in Treatment of Post-Burn Scars.

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Abstract: Objective: The purpose of this study was to evaluate the clinical and histopathological effects of fractional carbon dioxide laser alone versus fractional assisted corticosteroid delivery in treatment of post- burn scars. **Design:** This was randomized, blinded, clinically split scar Study **Setting:** The setting for this study was Dermatology Department at Al-Azhar University in Cairo, Egypt. **Participants**: Thirty patients with mature burn scars were included in the study. **Measurements:** Twelve fractional carbon dioxide laser sessions followed by application of triamcinolone acetonide suspension on half of the scar then other half treated by fractional CO2 laser alone were done 4 to 6 weeks apart. **Outcome Measures: Primary outcome** was measured using two scar scales, the Vancouver Scar Scale and the university of north Carolina scar score. Secondary outcomes included evaluation of collagen and elastic fibers using routine hematoxylin and eosin, Masson's trichrome, and orcein stains. Outcomes were measured one month after the last laser session**.** Results: Both Vancouver Scar Scale and the university of north Carolina scar score showed significant reduction following treatment (p<0.001). area of the scar treated by fractional carbon dioxide laser followed by application of triamcinolone acetonide suspension improved more than the other area treated by fractional CO2 laser alone but the improvement still not significant (p-value > 0.05). The pattern and arrangement of collagen and elastic fibers showed significant improvement (p<0.001, p=0.001, respectively), together with significant improvement in their amounts (p=0.020, p<0.001, respectively). Histopathological improvement was significant in area of the scar treated by fractional carbon dioxide laser followed by application of triamcinolone acetonide suspension more than the other area treated by fractional CO2 laser alone area (p<0.001). **Conclusion**: Fractional CO2 laser assisted topical steroid delivery could be considered as a promising option for burn scar management as it improves the clinical appearance of the scar, which was detected histologically by changing the dermal collagen orientation and thickness making it much similar to normal skin.
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Keywords: Fractional Carbon Dioxide Laser; Topical steroid delivery; Treatment; Post-Burn Scars

1. Introduction

Scars frequently cause both functional and esthetical problems ***(Van Loey et al., 2008).*** Cosmetic disfigurement caused by scars may lead patients to suffer from psychosocial problems, which in turn may result in a decreased quality of life ***(Bock et al., 2006).***

Scars are normally classified according to their clinical behavior and appearance. They are frequently categorized as normotrophic, hypertrophic, and keloidal ***(Verhaegen et al., 2009).***

Standard treatments for burn scars include excision, ultrasound, compression therapy, tissue expanders, silicone gel sheeting, intralesional steroids, interferon injections, and laser treatments ***(Xie et al., 2004).***

Fractional ablative carbon dioxide laser (AFXL) is a viable treatment option for scars ***(Anderson et al.,2014).*** AFXL generates vertical microscopic columns of tissue ablation in the epidermal and dermal layers, leaving intervening tissue intact. Each ablated channel is surrounded by a zone of thermally damaged skin. AFXL exposure elicits a cascade of cytokines and growth factors, leading to activation of fibroblasts, induction of neocollagenesis, and synthesis of elastin fibers. This pathway is assumed to promote structural changes in scar tissue ***(Ozog et al., 2013)***.

Fractional lasers create zones of ablation at variable depths determined by the treatment settings. The unique fractional injury induces a molecular cascade including heat shock proteins and other factors that lead to a rapid healing response and prolonged neocollagenesis with subsequent collagen remodeling ***(Waibel et al., 2009)***. When applied in a fractional pattern, columns of abnormal scar are ablated, allowing new collagen to form in a controlled manner, with rapid epithelialization of surface. Recent work suggests that in addition to

apoptosis of fibroblasts in the semicro thermal zones, or "MTZs," the hypertrophic scars undergo up regulation of matrix metalloproteinase 1 with alteration of types 1 and 3 procollagen levels and down-regulation of transforming growth factors and basic fibroblast growth factor. Not only are these changes evident in the MTZs, but the entire thickness of the dermis seems to be affected ***(Qu et al., 2012).***

Effective topical delivery of any pharmaceutical agent requires the ability to penetrate the epidermis. Fractional laser therapy creates precise, uniform columns of tissue vaporization which in theory might help to facilitate drug delivery past the epidermal barrier ***(Haedersdal et al., 2010)***.

Ablative fractional laser-assisted corticosteroid delivery may take advantage of the newly formed channels to penetrate uniformly and deeply into dermal scars. Furthermore, injection of triamcinolone acetonide is often painful and consistent dosing is difficult to achieve throughout the scar. In contrast, topical application of triamcinolone acetonide after fractional resurfacing is painless and may be applied with greater uniformity ***(Haedersdal et al., 2010)***.

Aim of the work

The aim of this study was to evaluate the clinical and histopathological effects of fractional carbon dioxide laser alone versus fractional assisted corticosteroid delivery in treatment of post- burn scars.

2. Patients and Methods

Patients:

The present study included **30** patients **(**16males (53,3%) and 14 females (46,7%)**)** with Fitzpatrick skin phototypes II-V; Patients with burn scars presenting to the outpatient clinic of the Dermatology Department at Al-Azhar University hospitals from June 2017 to July 2019 were screened for eligibility of enrollment in the trial. Included in the trial patients with burn scars that were at least one year old.

Exclusion criteria for enrollment were recent burn scars, pregnancy, lactation, oral retinoid drugs within the past 6 months and patients unable to follow the treatment protocol.

Methods:

The following items were completed for all patients:

• An informed consent before enrollment approved by our dermatology research ethical committee.

• Full history taking and full dermatological examination. Personal history was taking including name, age, sex, occupation and residence. History of present illness included the cause, site, duration of the burn scars, and previous treatment modalities used was documented for each patient.

• Dermatological examination was done to detect the type of Scar, site and extent of the lesion.

• The treated Scars were divided into two parts:

A-The first part was treated by fractional co2 laser followed by topical application of triamcinolone acetonide suspension at a concentration of 10-20mg /ml. The chosen concentration of triamcinolone acetonide was dependent on the extent and thickness of the scar. **(Group 1)**

B-The Second part was treated by fractional co2 laser alone**. (Group 2)**

Laser treatment. The target scars underwent twelve treatment sessions using a fractional ablative 10,600 nm CO2 laser (SmartXide DOT®; DEKA, Florence, Italy). Sessions were performed 4 to 6 weeks apart. Topical anesthesia (lidocaine 2.5% and prilocaine 2.5%) was applied to the target area 30 to 60 minutes before the procedure, and then the area was washed off and properly dried before laser application. The following parameters were used in a single pass (in all cases): power, 17 Watts; dwell time, 400µsec; stacking, 2; and spacing, 700µm.

Within 2 minutes of fractional laser treatment, a thin layer of triamcinolone acetonide suspension was drizzled over the site and rubbed gently over the ablated columns.

Post-laser home treatment included topical application of panthenol 2% twice daily for four weeks. Patients were also instructed to use sunscreen regularly (for scars in sun-exposed sites) and to avoid removal of the crust.

(3) Photography

All photographs were taken with a Nikon Power Shot D5300 digital camera (13.5 mega pixel resolution) using identical lighting situation and patient positioning. The photos were taken before starting treatment and one month after the last session. Two investigators were performed the assessment, but they were blinded to previous measurements and treatment regimens.

(4) Histological Evaluation

A pre-treatment, 4mm punch biopsy was taken from the target scar of each subject. A post-treatment two biopsies were taken one month after the last session (one from the part was treated by fractional Co2 laser followed by application of triamcinolone acetonide suspension and the second biopsy from the part was treated by fractional Co2 laser alone). Each patient was instructed to use topical and/or systemic antibiotic after the biopsy taking. Skin biopsies were collected in 10 % formaline, processed into paraffin blocks and cut into 7 µm paraffin sections that were subjected to the following stains:

o Hematoxylin and eosin for routine histological evaluation.

o Masson's Trichrome stain for collagen fibers.

o Orceinstain for elastic fibers.

Data management and statistical analysis:

Clinical and morphometric histological data were coded and entered to an excel spread sheet. All statistical calculations were done using computer programs SPSS version 15, 2010 for Microsoft Windows (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA). The data were statistically described in terms of mean ± standard deviation (±SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Mann Whitney U test for independent samples. Within group comparison of numerical variables was done using Wilcoxon signed rank test for paired (matched) samples when not normally distributed. For comparing categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. Within group comparison was done using McNemar test. P values less than 0.05 was considered statistically significant.

3. Results

In our study, we applied fractional co2 laser on 30 patients had mature burn scar, 16 males (53,3%) and 14 females (46,7%),. Their age ranged from 10 - 44 years, their Fitzpatrick skin phototypes II-V, duration of burn ranged from (2-9years) (**Table 1**).

Table 1: Demographic data of the patients with burn scar

No.	Age (Years)	Sex	Scar Duration (Years)	Burn Type	Site	Fitzpatrick Skin Type	Previous Treatment
1	20	F	2	Scald	Thigh	III	none
2	13	m	3	Fire	Arm	III	none
3	24	m	3	Scald	Arm	IV	Intralesional steroids
4	16	M	2	Fire	Arm	II	Intralesional steroids
5	15	M	2	Scald	Arm	V	none
6	31	F	5	Fire	Arm	III	none
7	27	M	2	Fire	Arm	IV	Intralesional steroids
8	19	F	3	Scald	Arm	IV	None
9	21	F	2	Fire	Breast	III	None
10	15	F	3	Scald	Abdomen	III	None
11	19	M	2	Scald	Arm	IV	Topical therapies
12	18	F	5	Fire	Chest	IV	None
13	41	F	9	Scald	Arm	II	Grafting
14	11	m	3	Fire	Arm	III	None
15	24	F	2	Fire	Thigh	III	None
16	19	F	6	Scald	Arm	III	Surgical release
17	18	F	3	Scald	Arm	III	None
18	17	F	2	Scald	Arm	II	None
19	44	F	4	Fire	Chest	III	None
20	32	M	3	Scald	Arm	IV	None
21	10	M	3	scald	Thigh	III	Topical therapies
22	13	M	3	Scald	Face	III	none
23	25	F	6	Scald	Back	IV	Intralesional steroids
24	16	M	2	scald	Arm	III	None
25	17	M	2	Fire	Face	III	None
26	22	M	3	Fire	Back	IV	Topical therapies
27	11	M	4	Scald	Thigh	IV	Topical therapies
28	14	F	3	Scald	Back	IV	Topical therapies
29	10	M	2	Scald	Face	III	Topical therapies
30	15	m	2	scald	Arm	III	None

Table (2): description of demographic data of studied patients.

Demographic data		Studied patients (N = 30)	
Age (years)	Mean ±SD	19.9 ± 8.4	
	Min - Max	10 – 44	
Sex	Male	16	53.3%
	Female	14	46.7%

According to clinical assessment, the results as follow:

Table (2) shows the description of demographic data of studied patients. **As regard age,** the mean age of studied patients was 19.9 ± 8.4 years with minimum age of 10 years and maximum age of 44 years. **As regard sex,** there were 16 males (53.3%) and 14 females (46.7%) in the studied patients.

Table (3) shows the description of clinical data of studied patients.

As regard duration of scar, the mean duration was 3.2± 1.6 years with minimum duration of 2 years and maximum duration of 9 years.

Table (3): description of clinical data of studied patients.

Clinical data		**Studied patients (N = 30)**	
Duration of scar (years)	**Mean ±SD**	3.2 ± 1.6	
	Min - Max	2 – 9	
The Cause of Burn	**Fire**	11	36.7%
	Scald	19	63.3%
Site of scar	**Face**	3	10%
	Chest	2	6.7%
	Breast	1	3.3%
	Arm	16	53.3%
	abdomen	1	3.3%
	Back	3	10%
	Thigh	4	13.3%
Fitzpatrick skin type	**II**	1	3.3%
	III	17	56.7%
	IV	7	23.3%
	V	5	16.7%
Previous treatment	**none**	17	56.7%
	Topical therapies	6	20%
	Intra-lesional steroids	5	16.7%
	Surgical release	1	3.3%
	Grafting	1	3.3%

Table (4): shows highly statistical significant difference **(p-value < 0.001)** of VSS (vascularity, pigmentation, pliability & height) between (before & group I).

Table (4): comparison of VSS between (before & group I).

VSS		**Before (N = 30)**		**Group I (N = 30)**		X^2	**P-value**
Vascularity	**Normal**	2	6.7%	20	66.7%	28.1	**< 0.001 HS**
	Pink	16	53.3%	10	33.3%		
	Red	10	33.3%	0	0%		
	Purple	2	6.7%	0	0%		
Pigmentation	**Normal**	2	6.7%	4	13.3%	37.9	**< 0.001 HS**
	Hypo	4	13.3%	25	83.3%		
	Hyper	24	80%	1	3.3%		
Pliability	**Supple**	0	0%	5	16.7%	25.8	**< 0.001 HS**
	Yielding	4	13.3%	18	60.0%		
	Firm	12	40%	5	16.7%		
	Banding	14	46.7%	2	6.7%		
Height	**< 2 mm**	0	0%	6	20.0%	48.8	**< 0.001 HS**
	2 – 5 mm	2	6.7%	23	76.7%		
	> 5 mm	28	93.3%	1	3.3%		

X^2: Chi-square test HS: p-value < 0.001 is considered highly significant.

Table (5) shows: Highly statistical significant difference **(p-value < 0.001)** of UNC4P (pruritus, pain, Paresthesia & pliability) between (before & group I).

Table (5): comparison of UNC4P between (before & group I).

UNC4P		Before (N = 30)		Group I (N = 30)		X^2	P-value
Pruritus	**Non**	0	0%	15	50%	30.8	**< 0.001 HS**
	Mild	10	33.3%	15	50%		
	Moderate	18	60%	0	0%		
	Severe	2	6.7%	0	0%		
Pain	**Non**	0	0%	19	63.3%	35.4	**< 0.001 HS**
	Mild	14	46.7%	11	36.7%		
	Moderate	14	46.7%	0	0%		
	Severe	2	6.7%	0	0%		
Paresthesia	**Non**	0	0%	28	93.3%	52.6	**< 0.001 HS**
	Mild	26	86.7%	2	6.7%		
	Moderate	4	13.3%	0	0%		
Pliability	**Non**	0	0%	8	26.7%	18.1	**< 0.001 HS**
	Mild	12	40%	18	60%		
	Moderate	18	60%	4	13.3%		

X^2: Chi-square test HS: p-value < 0.001 is considered highly significant. S: p-value < 0.05 is considered significant.

Table (6) shows highly statistical significant difference **(p-value < 0.001)** of histopathology (dermal thickness, collagen orientation, collagen morphology, elastic density & elastic morphology) between (before & group I).

Table (6): comparison of histopathology between (before & group I).

Histopathology		Before (N = 30)		Group I (N = 30)		X^2	P-value
Dermal thickness	+	0	0%	16	53.3%	40.0	**< 0.001 HS**
	++	0	0%	8	26.7%		
	+++	30	100%	6	20%		
Collagen orientation	**No change**	30	100%	2	6.7%	52.5	**< 0.001 HS**
	Mild imp.	0	0%	8	26.7%		
	Moderate imp.	0	0%	20	66.7%		
Collagen morphology	**No change**	30	100%	10	33.3%	30.0	**< 0.001 HS**
	Mild imp.	0	0%	20	66.7%		
Elastic density	**No change**	30	100%	6	20%	40.0	**< 0.001 HS**
	Mild imp.	0	0%	8	26.7%		
	Moderate imp.	0	0%	16	53.3%		
Elastic morphology	**No change**	30	100%	14	46.7%	21.8	**< 0.001 HS**
	Mild imp.	0	0%	8	26.7%		
	Moderate imp.	0	0%	8	26.7%		

X^2: Chi-square test HS: p-value < 0.001 is considered highly significant.

Table (7) shows highly statistical significant difference **(p-value < 0.001)** of VSS (vascularity, pigmentation, pliability & height) between (before & group II).

Table (7): comparison of VSS between (before & group II).

VSS		Before (N = 30)		Group II (N = 30)		X^2	P-value
Vascularity	**Normal**	2	6.7%	18	60%	25.4	**< 0.001 HS**
	Pink	16	53.3%	12	40%		
	Red	10	33.3%	0	0%		
	Purple	2	6.7%	0	0%		
Pigmentation	**Normal**	2	6.7%	2	6.7%	28.6	**< 0.001 HS**
	Hypo	4	13.3%	24	80%		
	Hyper	24	80%	4	13.3%		
Pliability	**Supple**	0	0%	4	13.3%	18.8	**< 0.001 HS**
	Yielding	4	13.3%	16	53.3%		
	Firm	12	40%	6	20%		
	Banding	14	46.7%	4	13.3%		
Height	**< 2 mm**	0	0%	4	13.3%	38.7	**< 0.001 HS**
	2 – 5 mm	2	6.7%	22	73.3%		
	> 5 mm	28	93.3%	4	13.3%		

X^2: Chi-square test HS: p-value < 0.001 is considered highly significant.

Table (8) shows highly statistical significant difference **(p-value < 0.001)** of UNC4P (pruritus, pain & Paresthesia) between (before & group II). Statistically significant difference **(p-value < 0.05)** of UNC4P (pliability) between (before & group II).

Table (8): Comparison of UNC4P between (before & group II).

UNC4P		Before (N = 30)		Group II (N = 30)		X^2	P-value
Pruritus	Non	0	0%	10	33.3%	33.3	< 0.001 HS
	Mild	10	33.3%	20	66.7%		
	Moderate	18	60%	0	0%		
	Severe	2	6.7%	0	0%		
Pain	Non	0	0%	16	53.3%	32.0	< 0.001 HS
	Mild	14	46.7%	14	46.7%		
	Moderate	14	46.7%	0	0%		
	Severe	2	6.7%	0	0%		
Paresthesia	Non	0	0%	26	86.7%	46.1	< 0.001 HS
	Mild	26	86.7%	4	13.3%		
	Moderate	4	13.3%	0	0%		
Pliability	Non	0	0%	6	20%	10.4	0.005 S
	Mild	12	40%	16	53.3%		
	Moderate	18	60%	8	26.7%		

X^2: Chi-square test HS: p-value < 0.001 is considered highly significant. S: p-value < 0.05 is considered significant.

Table (9) shows highly statistical significant difference **(p-value < 0.001)** of histopathology (dermal thickness, collagen orientation, collagen morphology, elastic density & elastic morphology) between (before & group II).

Table (9): comparison of histopathology between (before & group II).

Histopathology		Before (N = 30)		Group II (N = 30)		X^2	P-value
Dermal thickness	+	0	0%	8	26.7%	40.0	< 0.001 HS
	++	0	0%	16	53.3%		
	+++	30	100%	6	20%		
Collagen orientation	No change	30	100%	10	33.3%	30.0	< 0.001 HS
	Mild imp.	0	0%	20	66.7%		
Collagen morphology	No change	30	100%	18	60%	15.0	< 0.001 HS
	Mild imp.	0	0%	12	40%		
Elastic density	No change	30	100%	12	40%	25.7	< 0.001 HS
	Mild imp.	0	0%	16	53.3%		
	Moderate imp.	0	0%	2	2.7%		
Elastic morphology	No change	30	100%	14	46.7%	21.8	< 0.001 HS
	Mild imp.	0	0%	16	53.3%		

X^2: Chi-square test HS: p-value < 0.001 is considered highly significant.

Table (10) shows no statistical significant difference **(p-value > 0.05)** of VSS (vascularity, pigmentation, pliability and height) between (group I & group II).

Table (10): comparison of VSS between (group I & group II).

VSS		Group I (N = 30)		Group II (N = 30)		Stat. test	P-value
Vascularity	Normal	20	66.7%	18	60%	X^2=0.28	0.592 NS
	Pink	10	33.3%	12	40%		
Pigmentation	Normal	4	13.3%	2	6.7%	X^2 = 2.5	0.288 NS
	Hypo	25	83.3%	24	80%		
	Hyper	1	3.3%	4	13.3%		
Pliability	Supple	5	16.7%	4	13.3%	X^2=0.99	0.804 NS
	Yielding	18	60.0%	16	53.3%		
	Firm	5	16.7%	6	20%		
	Banding	2	6.7%	4	13.3%		
Height	< 2 mm	6	20.0%	4	13.3%	X^2 = 2.22	0.329 NS
	2 – 5 mm	23	76.7%	22	73.3%		
	> 5 mm	1	3.3%	4	13.3%		

X^2: Chi-square test NS: p-value > 0.05 is considered non-significant. MW: Mann-Whitney Test

Table (11) shows no statistical significant difference **(p-value > 0.05)** of UNC4P (pruritus, pain, pliability & Paresthesia) between (group I & group II).

Table (11): comparison of UNC4P between (group I & group II).

UNC4P		Group I (N = 30)		Group II (N = 30)		X^2	P-value
Pruritus	**Non**	15	50%	10	33.3%	1.7	0.190 NS
	Mild	15	50%	20	66.7%		
Pain	**Non**	19	63.3%	16	53.3%	0.617	0.432 NS
	Mild	11	36.7%	14	46.7%		
Paresthesia	**Non**	28	93.3%	26	86.7%	0.74	0.389 NS
	Mild	2	6.7%	4	13.3%		
Pliability	**Non**	8	26.7%	6	20%	1.73	0.419 NS
	Mild	18	60%	16	53.3%		
	Moderate	4	13.3%	8	26.7%		

X^2: Chi-square test NS: p-value > 0.05 is considered non-significant.

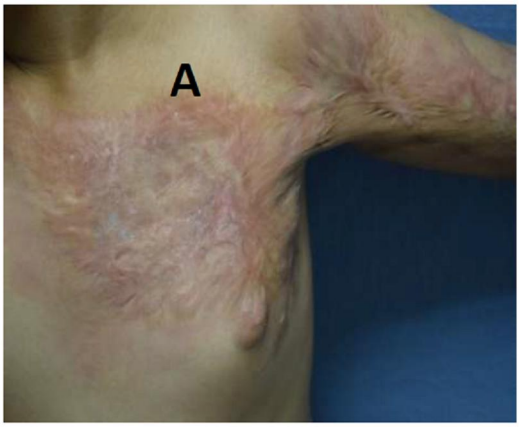
Table (12) shows Highly statistical significant difference **(p-value < 0.001)** of histopathology (collagen orientation & elastic density) between (group I & group II).

Table (12): comparison of histopathology between (group I & group II).

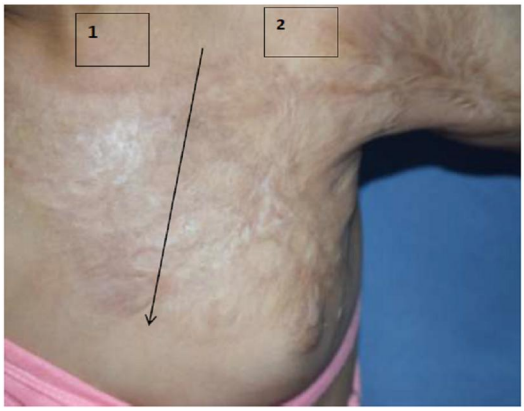
Histopathology		Group I (N = 30)		Group II (N = 30)		X^2	P-value
Dermal thickness	+	16	53.3%	8	26.7%	5.3	0.069 NS
	++	8	26.7%	16	53.3%		
	+++	6	20%	6	20%		
Collagen orientation	**No change**	2	6.7%	10	33.3%	30.5	**< 0.001 HS**
	Mild imp.	8	26.7%	20	66.7%		
	Moderate imp.	20	66.7%	0	0%		
Collagen morphology	**No change**	10	33.3%	18	60%	4.3	**0.038 S**
	Mild imp.	20	66.7%	12	40%		
Elastic density	**No change**	6	20%	12	40%	15.6	**< 0.001 HS**
	Mild imp.	8	26.7%	16	53.3%		
	Moderate imp.	16	53.3%	2	2.7%		
Elastic morphology	**No change**	14	46.7%	14	46.7%	10.7	**0.005 S**
	Mild imp.	8	26.7%	16	53.3%		
	Moderate imp.	8	26.7%	0	0%		

X^2: Chi-square test HS: p-value < 0.001 is considered highly significant. NS: p-value > 0.05 is considered non-significant. S: p-value < 0.05 is considered significant.

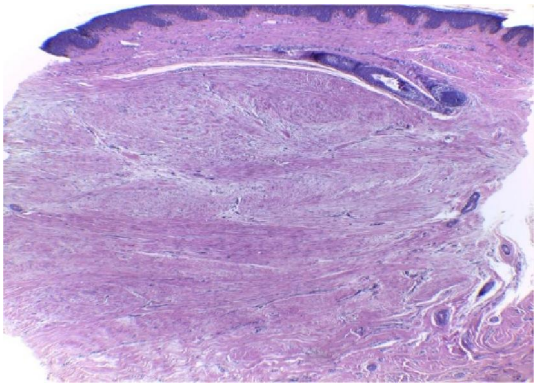
- Statistically significant difference **(p-value < 0.05)** of histopathology (collagen morphology & elastic morphology) between (group I & group II).
- No statistical significant difference **(p-value > 0.05)** of histopathology (dermal thickness) between (group I & group II).



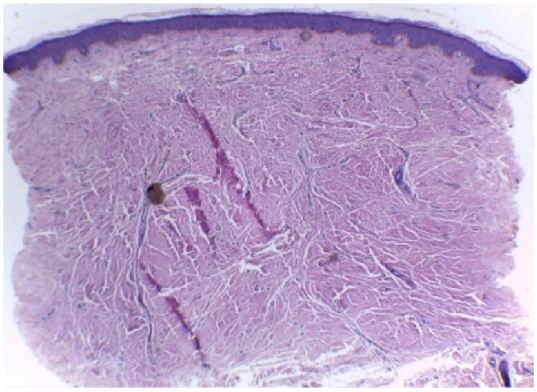
A) The patient before treatment



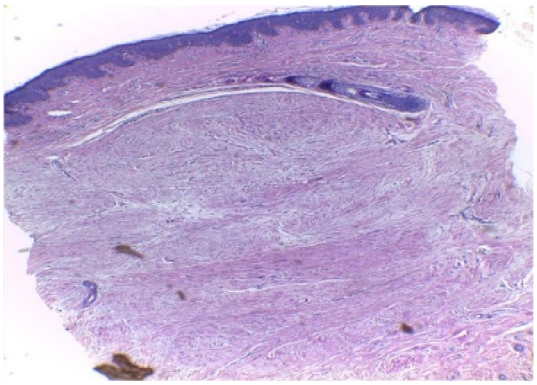
Patient after treatment (***area 1*** treated by fractional co2 laser followed by triamicinoloneacetonide, ***area 2*** treated by fractional laser alone).



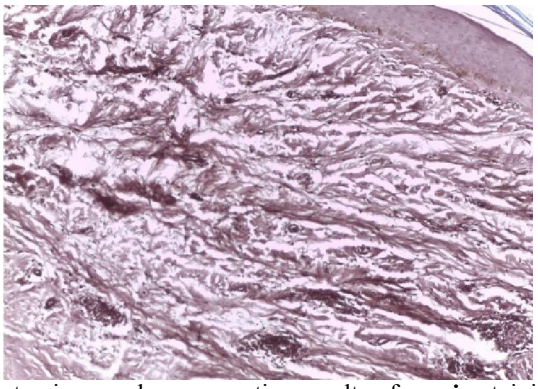
Photomicrograph demonstrating histopathological changes of collagen fibers using routine H & E stain, before treatment show The thick sclerotic collagen bundles in the scar tissue, loss of orientation and increasing of dermal thickness before treatment.



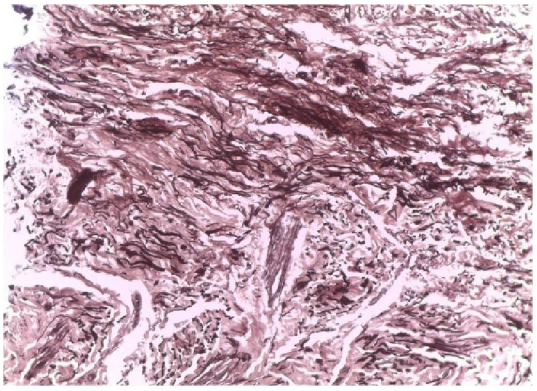
Photomicrograph demonstrating histopathological changes of collagen fibers using routine H & E stain, after treatment by fractional co2 laser followed by triamicinoloneacetonide, The thick sclerotic collagen bundles in the scar tissue before treatment changed to a combination of fibrotic and fibrillar collagen, with vessels starting to appear in the scar tissue perpendicular to the epidermis after treatment.



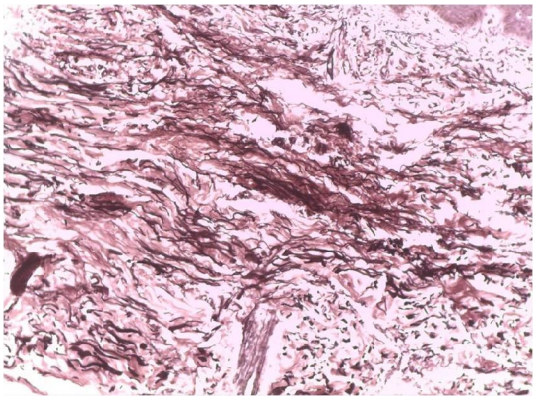
Photomicrograph demonstrating histopathological changes of collagen fibers using routine H & E stain, after treatment by fractional co2 laser alone. The thick sclerotic collagen bundles in the scar tissue before treatment changed to a combination of fibrotic and fibrillarcollagen.



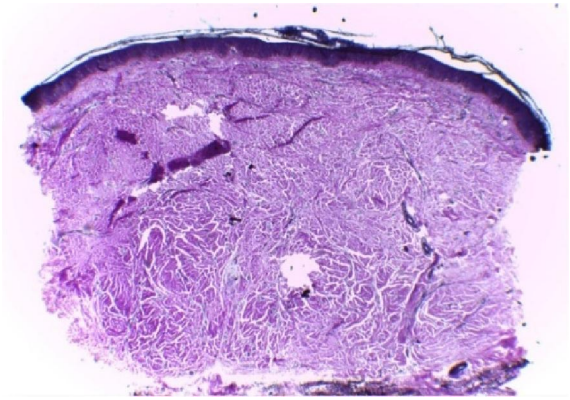
Photomicrographs representing results of **orcein** staining for elastic fibers for the same case **before** treatment. Elastic fibers were completely absent from the scar tissue before treatment



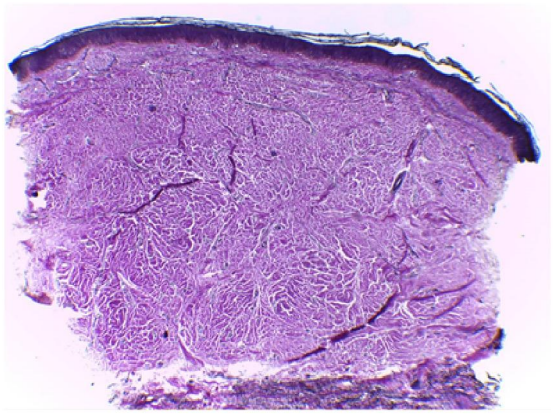
Photomicrograph representing results of orcein staining for elastic fibers for the same case after treatment by fractional co2 laser followed by triamicinoloneacetonide Elastic fibers were started to appear as a combination of short fragmented and fibrillar fibers.



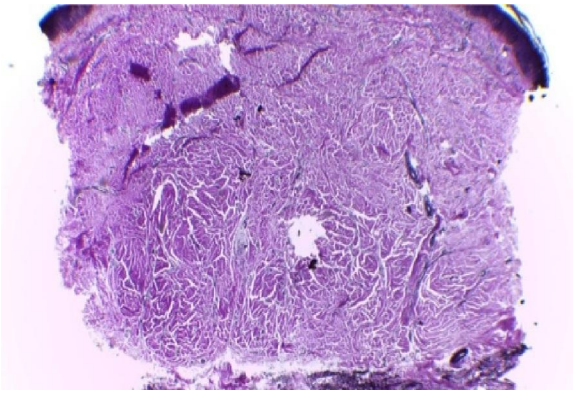
Photomicrographs representing results of orcein staining for elastic fibers for the same case after treatment fractional co2 laser alone, Elastic fibers started to appear as a combination of short fragmented and fibrillar fibers.



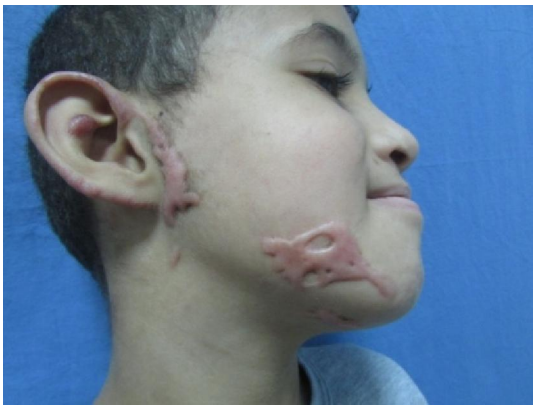
Photomicrograph representing results of Masson's trichrome staining for collagen fibers for the same case, before treatment show collagen density.



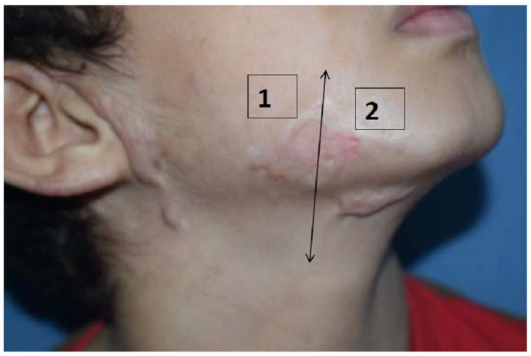
Photomicrograph representing results of Masson's trichrome staining for collagen fibers for the same case after treatment by fractional co2 laser followed by triamicinoloneacetonide show Reduction in collagen density and improved collagen quality.



Photomicrograph representing results of Masson's trichrome staining for collagen fibers for the same case after treatment by fractional co2 laser alone Reduction in collagen density and improved collagen quality.



The patient before treatment.



Patient after treatment (***area 1*** treated by fractional co2 laser followed by triamicinoloneacetonide, ***area 2*** treated by fractional laser alone).

4. Discussion

Fractional ablative carbon dioxide laser (AFXL) is a viable treatment option for scars ***(Anderson et al., 2014).*** AFXL generates vertical microscopic columns of tissue ablation in the epidermal and dermal layers, leaving intervening tissue intact. Each ablated channel is surrounded by a zone of thermally damaged skin. AFXL exposure elicits a cascade of cytokines and growth factors, leading to activation of fibroblasts, induction of neocollagenesis, and synthesis of elastin fibers. This pathway is assumed to promote structural changes in scar tissue ***(Ozog et al., 2013)***.

Fractional lasers create zones of ablation at variable depths determined by the treatment settings. The unique fractional injury induces a molecular cascade including heat shock proteins and other factors that lead to a rapid healing response and prolonged neocollagenesis with subsequent collagen remodeling ***(Waibel et al., 2009)***. When applied in a fractional pattern, columns of abnormal scar are ablated, allowing new collagen to form in a controlled manner, with rapid epithelialization of surface. Recent work suggests that in addition to apoptosis of fibroblasts in these micro thermal zones, or "MTZs," the hypertrophic scars undergo up regulation of matrix

metalloproteinase 1 with alteration of types 1 and 3 procollagen levels and down-regulation of transforming growth factors and basic fibroblast growth factor. Not only are these changes evident in the MTZs, but the entire thickness of the dermis seems to be affected ***(Qu et al., 2012).***

Effective topical delivery of any pharmaceutical agent requires the ability to penetrate the epidermis. Fractional laser therapy creates precise, uniform columns of tissue vaporization which in theory might help to facilitate drug delivery past the epidermal barrier ***(Haedersdal et al., 2010)***.

Ablative fractional laser-assisted corticosteroid delivery may take advantage of the newly formed channels to penetrate uniformly and deeply into dermal scars. Furthermore, injection of triamcinolone acetonide is often painful and consistent dosing is difficult to achieve throughout the scar. In contrast, topical application of triamcinolone acetonide after fractional resurfacing is painless and may be applied with greater uniformity ***(Haedersdal et al., 2010)***.

Since combination therapy may result in synergistic effects and regarding the lack of studies on this issue, the current investigation was performed to determine the comparative effects of ablative fractional CO2 laser plus triamcinolone acetonide suspension versus ablative fractional CO2 laser alone in the treatment of post burn scars.

In this randomized, blinded, clinically split scar study, objective assessment of the pigmentation, erythema, pliability, and height was done using the Vancouver scar score.

Subjective assessment of the pain, pruritus, parathesia and pliability was done using the university of north Carolina scar score.

Objective measures showed significant improvement of the burn scars following fractional CO2 laser treatment. This was in agreement with the findings of several researchers using different parameters. ***Waibel et al, (2009); Ozog et al, (2013); El-Zawahry et al. (2015) and El-Hoshy et al. (2017).***

Subjective measures showed a significant change in the opinion of the patients about their scar appearance. This was in agreement with ***Hultman et al. (2014).***

In the current study, improvement was higher for part of the scar treated by fractional CO2 laser plus triamcinolone acetonide than part of the scar treated by fractional CO2 laser alone clinicaly and histopathological but this improvement non significant.

In the current study, improvement was significantly higher for pliability, vascularity, height and pigmentation. This was similar to the finding by ***Kim et al, (2014)*** who reported that ablative fractional CO2 laser use was more effective in improving pliability and thickness of surgical scars, while pulsed dye laser (PDL) use was superior regarding treating vascularity and pigmentation. This suggests that firm, irregular scars are the best candidates to respond to fractional CO2 laser use rather than erythematous, hyperpigmented ones. The initial management of hyperemic scars by PDL targeting the vasculature, followed by the fractional CO2 laser, might be a more suitable plan for managing hyperemic scars.

The significant improvement in scar thickness and pliability achieved by fractional CO2 use in our study was shown by histological analysis to be due to its effect on collagen and elastic fibers.

Improvement in scar vascularity by fractional CO2 lasers occurred in our cases and this might be explained by the dermal blood vessels becoming less trapped and more perpendicular to the epidermis as a result of collagen remodeling. This observation was also reported by both ***Ozog et al, (2013), Makboul et al, (2014)*** and ***El-Hoshy et al. (2017).***

Targeting tissue water may lead to thermally induced destruction of the blood vessels ***Glaich et al, (2007)*** with subsequent improvement of erythema.

In both Masson's trichrome and orceinstained samples, the irregular sclerotic collagen fibers significantly changed to less sclerotic, finer, more fibrillar collagen, with a significant reduction in the amount of collagen fibers. Our findings were in agreement with ***Ozog et al, (2013); Makboul et al, (2014); El-Zawahry et al. (2015) and El-Hoshy et al. (2017).***

Fractional CO2 laser induces matrix metalloproteinases (MMPs), which clear the damaged collagen and allow for collagen remodeling to take place, with the formation of new, healthy collagen. (***Reilly et al, 2010***).

A significant improvement in morphology and orientation of elastic fibers was detected in the current study, the amount of elastic fibers increased significantly after treatment. ***Ozog et al, (2013) and El-Hoshy et al. (2017))*** reported similar changes.

In contexts other than burn scars, ***Shin et al (2011)*** reported increased density of elastic fibers following fractional CO2 laser treatment of striaedistensae. Also***, Jiang et al (2014)*** performed a single pass fractional CO2 laser session on mice dorsal skin and detected the replacement of lumps of old elastic fibers by slender elastic fibers with a wider distribution within few hours of fractional CO2 resurfacing.

The age of the patient, the scar site and scar duration have been found no differences in the efficacy of treatment. Also ***Haedersdal et al (2009)*** found no differences in the efficacy of treatment with respect to subject age, anatomical location of the scar, or duration of the scar. On the other hand the shorter

the scar duration, the better the improvement with fractional CO2 laser. This finding is reiterated in the observation reported by ***Niwa et al, (2009)*** stating that scars less than one year in duration improve more noticeably. This is mostly due to the effect of cytokines and growth factors that influence fibroblast activity early on in wound healing. In treating different types of scar, ***El Taweel and Abd El-Rahman (2014)*** found that clinical improvement was better in younger patients.

Laser plus triamcinolone treatment was more effective on texture and homogenous status in our study. ***Waibel et al. (2013)*** also demonstrated good response of texture in patients under treatment with laser plus triamcinolone.

The present study has confirmed that clinical improvement of burn scars after fractional CO2 laser treatment is mirrored by histologic findings, which showed an increased epidermal thickness, thinning in the stratum corneum and replacement of the irregular dermal collagen bands with organized parallel new collagen fibrils making it more closely resembling that of normal skin.

Similar to our results, ***Bonan et al. (2013)*** reported that laser makes dermal collagen finer and less dense. They claimed that ischemia from microvascular destruction caused by laser releases collagenase which leads to collagenolysis. Also dermal heat produced from blood vessels irradiated by laser can stimulate the collagen synthesis and remodeling. TGF-b1 has been shown to play an important role in the formation of hypertrophic scar.

Conclusion

Fractional CO2 laser assisted topical steroid delivery could be considered as a promising option for burn scar management as it improves the clinical appearance of the scar, which was detected histologically by changing the dermal collagen orientation and thickness making it much similar to normal skin.

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