

# Assessment of Fibroblast growth factor-1 as a serum marker in patients with hypertrophic scars undergoing CO2 fractional laser

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## Abstract

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**Background** Fractional CO2 laser has shown a great efficacy for the treatment of hypertrophic scars; however, there are different levels of therapeutic outcomes depending on many factors. The aim of this study was to detect any relation between serum level of fibroblast growth factor-1 and the response of the hypertrophic scars to the treatment with fractional CO2 resurfacing. **Methods:** Twenty patients with hypertrophic scars were included in the study. A serum sample was taken from each patient to assess the serum level of fibroblast growth factor 1. Each patient was subjected to fractional carbon dioxide laser with a frequency of a session every month. Evaluation of the scars was done before starting treatment and after each 3 consecutive sessions by Vancouver score scale (VSS). **Results:** Analysis of the results showed that there is a statistically significant improvement of the hypertrophic scars by using fractional CO2 laser resurfacing, but the percent of improvement showed insignificant correlation with the age, body mass index (BMI) of patients and disease duration. Also, the results revealed that Serum fibroblast growth factor 1 had insignificant correlation with the percent of improvement of the scars treated. **Conclusion:** Serum fibroblast growth factor-1 can't be used as a marker to predict the probable response of the hypertrophic scars to the treatment with fractional CO2 laser.

**Keywords:** Hypertrophic scars, fractional CO2 laser, fibroblast growth factor 1

## INTRODUCTION

Hypertrophic scars are thick raised scars which are considered very common complications due to abnormal healing of wounds which may lead to disfigurement, loss of function, together with physical and mental stress. [1]

Hypertrophic scar formation usually starts by dermal injury that can be caused by burn, surgery, and trauma. This is followed by attracting the immune cells to the site of the scar healing. The immune cells may lead to hypertrophic scar formation by enhancing the inflammation at the wound site. Also, different growth factors can enhance cell functions as cell proliferation, angiogenesis, proliferation and fibrosis increasing the risk of abnormal wound healing resulting in excessive and rigid scarring. [2]

Treatments of hypertrophic scars usually aim to decrease the thickness, size and consistency of the scars and also improve their colour. The most common treatment modality is corticosteroid injection and bleomycin injection, but there is limited tolerability from the patients to this type of treatment, especially for large sized scars. [3]

Also topical preparation like silicone gel requires very long time of treatment with usually unacceptable outcome, thus the use of ablative lasers is usually a very good option as a fast, safe, effective modality of treatment for large resistant hypertrophic scars. [4, 5]

However, studies had shown variable improvement levels among patients that lead us to think about the presence of serum factors that may affect the efficacy of the lasers on the hypertrophic scars. [6]

Fibroblast growth factors belong to a large family of growth factors. They mediate angiogenesis, wound healing, embryonic development, and metabolism regulation. [7]

It was proved in previous studies that fibroblast growth factor receptor-1 was expressed during skin healing and during the step of epidermal regeneration and also expressed to some extent in the dermal capillaries so that it may be an indicator of the possible important role of fibroblast growth factor-1 during the treatment of hypertrophic scars by ablative techniques and subsequently the measurement of serum level of such growth factor may give a hint about the possible treatment outcome. [8]

This study was designed to evaluate if the serum level of fibroblast growth factor-1 may play a role as an intrinsic independent variable that affect the response of the hypertrophic scars to the treatment by the fractional CO<sub>2</sub> laser so can be used to predict the upcoming results before the start of such treatment modality. In order to prove this; we had to observe a correlation between the serum level of fibroblast growth factor-1 and the percentage of improvement of hypertrophic scars treated with fractional CO<sub>2</sub> resurfacing.

## PATIENTS AND METHOD

The study was an observational, cross-sectional study that was conducted after approval of the National Research Centre (NRC), Dermatology Department, Ethical committee (approval no; 01470324) with the principles outlined in the declaration of Helsinki for human subject experimentation being followed. Informed consent was obtained from the patients, and the privacy rights were continuously observed.

The study was conducted on twenty patients presenting with hypertrophic scars, diagnosed clinically, and recruited from the dermatology out-patient clinics of the National Research Centre (NRC). The patients were of both sexes and were above the age of 18 years.

### Exclusion criteria:

1. Patients with bleeding tendency
2. Patients receiving topical treatment for the last 2 weeks.
3. Pregnancy and Lactation.

### Methods:

Patients will be subjected to the following:

1. Informed written consent.
2. Thorough history taking and clinical evaluation.
3. At Visit 1, the hypertrophic scars were evaluated by clinical examination. Vancouver score scale (VSS) was calculated for the area of the scar to be treated and photographs were taken before the beginning of the treatment.
4. Three ml serum sample was taken from the patients under complete aseptic condition.
5. Serum fibroblast growth factor-1 was assessed for each patient by using FBGF-1 enzyme linked immunoassay (ELISA) kit in the labs of the national research centre.
6. Treatment of the hypertrophic scars was by the fractional ablative 10600nm CO<sub>2</sub> laser (BX3008:AMI Inc.). Sessions were performed with a frequency of one session every month by using the following parameters in a single pass, smart stack, dot mode, power: 45 mj, pulse duration: 200 microseconds, density level:15 step, depth level: 2, spot size: 17x17 mm.
7. Reevaluation of the hypertrophic scars after 3 laser sessions

### Patient evaluation

Every patient was evaluated before every session for 3 consecutive sessions using Vancouver score scale (VSS) as follows:

### Vancouver score scale

It is a scar assessment numeric score, widely used in clinical practice and researches. It depends on evaluation of four characteristics of the scar. These are: vascularity, height, pliability, and pigmentation. As shown in table 1, each characteristic is given a score and then added together to get the final score that ranges from 0 to 13. [9]

**Table (1) the Vancouver Score Scale (VSS)**

<b>Pigmentation (0-2)</b>	Normal	0
	Hypopigmentation	1
	Hyperpigmentation	2
<b>Vascularity (0-3)</b>	Normal	0
	Pink	1
	Red	2
	Purple	3
<b>Pliability (0-5)</b>	Normal	0
	Supple	1
	Yielding	2
	Firm	3
	Banding	4
	Contracture	5
<b>Height (0-3)</b>	Normal (flat)	0
	0-2 mm	1
	2-5 mm	2
	>5 mm	3

Also, the patients were asked about any side effects that might happen during the treatment.

### Statistical analysis

Analysis of data was done by IBM computer using SPSS (statistical program for social science version 23). Quantitative variables were described as Mean, SD, Median and IQR according to shapiro test of normality and qualitative variables were described as number and percentage.

Mann Whitney test was used to compare quantitative variables between two groups in non-parametric data (SD>30%mean) while Kruskal Wallis test was used to compare quantitative variables between more than two groups in non-parametric data (SD>30%mean). Also, Wilcoxon Signed Rank test used to compare pre and post variables in non-parametric data and Spearman correlation test used test for linear relations between variables where P value >0.05 insignificant and P value<0.05 significant. [10]

## RESULTS

Clinical and demographic characteristics of the 20 patients included in the study were shown in Table 2.

### Effect of the fractional CO<sub>2</sub> laser over the hypertrophic scars

For each patient, we interpreted the VSS after 3 sessions of treatment with fractional laser and there was a statistically significant improvement of the scars (p value ≤ 0.05) as shown in table 3.

Table (2): Demographic data of the patients

	Mean±SD	Median(IQR)	Range
Age (years)	33.7±3.63	34.5(30.5-37)	28-39
BMI	29.2±4.66	28(26-33)	21-39
Disease duration (years)	2.5±1.05	2(2-3)	1-5

Table (3): Comparison between VSS before and after treatment

	Pre	Post	p value
Vancouver score before			
Median(IQR)	9(7-9)	6.5(6-7)	<0.001
Range	4-9	4-8	

#### Relation between the percent of improvement and different patient variables

On studying the relation of the percent of improvement of scars with different variables including

age of patients, BMI, and duration of the scars, we didn't find any significant correlation between the analysed variables and the percent of improvement as shown in table 4.

Table (4): Relation between percent of improvement and patients variables

	Percent of improvement (%)	
	R	p value
Age (years)	-0.077	0.747
BMI	0.092	0.7
Disease duration (years)	0.017	0.944
Vancouver score before	0.413	0.07
Vancouver score after	-0.367	0.111
Serum fibroblast growth factor 1 (pg/ml)	-0.028	0.906

#### Relation between serum level of fibroblast growth factor-1 and percent of improvement

In our study, we couldn't find a significant relation between serum fibroblast growth factor-1 and the percent of improvement of scars under treatment with

fractional CO<sub>2</sub> laser while the significant relation between serum fibroblast growth factor 1 and other patient variables like BMI and age of patients that was reported in many previous studies was confirmed (table 5).

Table (5): Relation between serum fibroblast growth factor 1 and patients variables

	Serum fibroblast growth factor 1 (pg/ml)	
	R	p value
Age	.450*	<b>0.047</b>
BMI	.863**	<b>&lt;0.001</b>
Disease duration (years)	-0.039	0.87
Vancouver score before	-0.073	0.759
Vancouver score after	0.02	0.933
Percent of improvement (%)	-0.028	0.906

## DISCUSSION

In this research, we tried to find a relation between serum fibroblast growth factor-1 and the response of the hypertrophic scars to the treatment with fractional CO<sub>2</sub> laser so as to consider it as a prognostic factor that may affect the clinical and therapeutic decisions and also may help to find targets for new promising interventions for faster and more preferable outcome.

There are many studies that tested many factors; either related to the patients or related to the treatment protocol that may affect the response of the scars to treatment. Discovering these factors can help the physicians to predict the possible outcome so modifying the treatment plan.[11]

From a dermatologist's perspective, there are many studies that reported the important role of fibroblast growth factor-1 in the process of wound healing either

after injury or after ablation of the skin by the ablative lasers.[12] In the current manuscript, we attempted to measure the serum level of fibroblast growth factor-1; which is a subjective unchangeable variable, during the treatment of hypertrophic scars with fractional CO2 laser to identify if there is any significant correlation between it and the percent of improvement with this treatment modality.

As reported in the current study, there was no correlation between the serum level of fibroblast growth factor-1 and the rate of improvement of hypertrophic scars treated with fractional CO2 laser but to address that we can't use serum fibroblast growth factor-1 as a prognostic factor before the treatment of hypertrophic scars by fractional laser resurfacing, we recommend, based on previous scientific recommendations, to examine the prognostic ability of fibroblast growth factor-1 across multiple studies, and also to increase the use of meta-analysis of the patients data to get rid of any reporting bias and analysis defects.[13]

#### Declarations:

**Consent for publication:** Not applicable

**Availability of data and material:** Data are available upon request.

**Competing interests:** The author(s) declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article. This manuscript has not been previously published and is not under consideration in another journal.

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