Comparison of Fractional CO₂ Laser with Intralesional Verapamil versus Fractional CO₂ Laser with Intralesional Triamcinolone for the Treatment of Keloid

Sahar Mahsoub Mohammed Soliman Fayed*, Hanan Fathy Mohammed, Moheiddin Fakhry Alghobary

Department of Dermatology, Andrology and STDs, Faculty of Medicine, Mansoura University, Egypt

*Corresponding author: Sahar Mahsoub Mohammed, Mobile: (+20) 01155515220, E-Mail: smohaa100@yahoo.com

ABSTRACT

Background: Although keloids of unknown origin can also develop, keloids are a skin disease where the skin expands past the borders of the initial incision. Intralesional triamcinolone (TAC) injections have been demonstrated to lessen related scar pain and itching, decrease scar volume and height, and improve scar pliability. One of calcium channel blockers; verapamil, causes the release of procollagenase, which speeds up the breakdown of scar tissue. As a result, the morphology of fibroblasts changes, TGF-1 apoptosis is induced, the formation of extracellular matrix (ECM) is decreased, and actin filaments are depolymerized.

Objective: comparing the efficacy and safety of fractional CO_2 combined with intralesional verapamil versus fractional CO_2 combined with intralesional triamcinolone in the treatment of keloid.

Patients and methods: Twenty patients with keloids participated in this investigation. They were chosen from the Dermatology Department's Outpatient Clinic at Mansoura University Hospital. Patients with two keloid were recruited; one keloid was treated with fractional CO_2 with intralesional verapamil (arm A) and the other was treated with fractional CO_2 with intralesional triamcinolone (arm B).

Results: In the fractional CO₂ laser with intralesional triamcinolone and verapamil groups, there was a statistically significant decrease in the height and surface area of keloid before and after treatment. The reduction of lesion height was significantly higher in fractional CO₂ laser with intralesional triamcinolone group in comparison with verapamil group (P = 0.003).

Conclusion: Combined fractional CO_2 laser with intralesional triamcinolone therapy showed better clinical improvement compared to combined fractional CO_2 laser with intralesional verapamil therapy, but with more adverse effects.

Keywords: Treatment of Keloid, Fractional CO₂ Laser, Intralesional Verapamil, Intralesional Triamcinolone

INTRODUCTION

A benign fibroproliferative condition called a keloid is characterized by aberrant collagen deposition within a wound. This cutaneous "tumor" spreads past the edge of the initial lesion, grows over time, frequently returns after excision, and infrequently regresses on its own⁽¹⁾.

It is believed that increased collagen and ECM synthesis and decreased breakdown lead to the development of keloid lesions. The overexpression of inflammatory mediators, specifically TGF- β 1, is thought to be responsible for the increased synthesis of ECM collagen⁽²⁾.

Although there are many ways to treat keloids, none of them has been shown to be particularly successful⁽³⁾. The use of a fractional carbon dioxide laser has been the subject of more recent research⁽⁴⁾.

Both keloids and hypertrophic scars were treated in an early trial using CO_2 laser monotherapy (four treatments, six weeks apart). The findings were conflicting. Although a statistically significant decline in Vancouver-Scar-Scale (VSS) scores was observed (primarily due to greater pliability), many patients did not find this therapy to be effective⁽⁵⁾. In a case study, treatment with fractionated CO_2 laser and laser-assisted medication administration of topical triamcinolone resulted in scar shrinking and improved vision⁽⁶⁾.

It has been demonstrated that intralesional triamcinolone (TAC) injections can lessen related scar pain and itching while also reducing scar volume and height ⁽⁷⁾, as well as various rate of recurrency ⁽⁸⁾.

Verapamil, a calcium channel blocker, stimulates the release of procollagenase, which speeds up the breakdown of scar tissue. This modifies the morphology of fibroblasts, triggers TGF- β 1 apoptosis, lowers the formation of ECM, and depolymerizes actin filaments⁽⁹⁾. Verapamil administered intralesionally for the treatment of keloid scars is risk-free ⁽¹⁰⁾.

In order to treat keloid lesions, this study compares the effectiveness and safety of fractional CO_2 combined with intralesional verapamil with fractional CO_2 combined with intralesional triancinolone.

PATIENTS AND METHODS

Twenty patients with keloids were included in this comparative interventional investigation. They were chosen from the Mansoura University Hospitals' Dermatology, Urology, and STD Outpatient Clinic.

All studied patients had two keloid, one keloid was treated with fractional CO_2 with intralesional verapamil (arm A) and other was treated with fractional CO_2 with intralesional triamcinolone (arm B).

Ethical consent:

The Mansoura Faculty of Medicine's Institutional Review Board (IRB) accepted this research (MS.19.06.677). An informed consent was taken from every participant before inclusion of patients into the study. Every care was taken to protect the data's privacy. All data were used exclusively for scientific purposes. The Declaration of Helsinki, the World Medical Association's code of ethics for studies involving humans, guided the conduct of this research.

Inclusion criteria:

- Patients age: from 18 to 50 years
- Sex: male and female
- Duration of lesion: more than 6 month and less than 5 years
- Patients with two keloids.

Exclusion criteria:

- Pregnancy or lactating females.
- Patients who receives previous treatment for keloid in the past 12 months.
- Patients with chronic disease affecting wound healing (cardiovascular disease, diabetes, liver cell failure, malignancy and kidney disease).
- keloid results from burn.

Each patient was introduced to:

- Through history taking (personal, past, present, family history).
- Detailed general and dermatological examination.
- In patients, who were recruited as they had at least two keloids, lesion were divided in two arms of intervention according to their therapy plan:

Arm A: keloids were treated by fractional CO₂ with intralesional verapamil.

Arm B: keloids were treated by fractional CO₂ with intralesional triamcinolone.

Technique:

Arm A: lesion received combined treatment of fractional CO_2 laser with intralesional verapamil after 10 to 15 minutes at the same session for 4 successive sessions at monthly intervals. A maximum 2 mL of verapamil (2.5 mg/mL) was injected per session.

Arm B: Lesion received combined treatment of fractional CO_2 laser with intralesional triamcinolone after 10 to 15 minutes of laser session, for 4 successive session at monthly intervals. A maximum of 2 mL of triamcinolone (20 mg/mL) per session.

Laser apparatus and parameters:

Utilizing the following settings: Smart stack (10–15W), stack 3, (400–600 μ m) dwelling duration, and (400–600 μ m) spacing (DEKA, fractional CO₂ laser Smart-xide DOT, Italy). Before, after, and in between fractional CO₂ laser sessions, all patients got comprehensive instructions.

Before laser session: Before the laser treatment, a topical anesthetic cream (lidocaine 25 percent and prilocaine 25 percent pridocaine *R) was put under occlusion for 60 minutes..

Post laser session: Topical antibiotic, topical wound healing measures, emollients and sun screen in sun exposed areas.

Follow up:

Assessment of the efficacy of therapeutic procedure:

Photographs were obtained at baseline, standardized photographs were performed using the same digital camera set at a fixed distance from the patient's lesion without flash light of the camera and were taken before every session.

Vancouver-Scar-Scale (VSS) before each session was assessed. In the case of VSS, keloid height was measured using a digital caliper, pliability was determined by palpation, vascularity was determined by ocular inspection, and pigmentation was determined by blanching the area and comparing it to the surrounding skin. ⁽¹¹⁾. Before and after the final session, the total surface area of the keloid was measured using a caliper.

At the conclusion of sessions, patients were scored on a scale of 0 (not satisfied), 1 (somewhat satisfied), 2 (satisfied), 3 (very satisfied), and 4 (extremely satisfied).

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) application for Windows was used to analyse the data (Standard version 21).

The Kolmogorov-Smirnov test was initially used to determine whether the data were normal or not. Number and percentage were used to describe qualitative data.

Using the Chi-square test, associations between categorical variables were investigated. Quantitative variables were all non-parametric and were displayed as median (min-max) and were compared using the Mann Whitney test. Wilcoxon signed rank test was employed to compare the two matched groups. The level of significance for each of the aforementioned statistical tests was set at 5%. (pvalue).

RESULTS

The demographic data of the patients are shown in table 1.

		All patients (n= 20)	
Age (years)	Median (min-max)	22.00 (18, 46)	
Gender	Male	6 (30.0%)	
	Female	14 (70.0%)	
Socioeconomic class	Low	4 (20.0%)	
	Middle	11 (55.0%)	
	High	5 (25.0%)	
Family history		6 (30.0%)	
Data is expressed as median and range or as percentage and frequency.			

Table (1): Demographic characteristics of the studied patients

The median duration of keloid lesion was 12 months. The median length of keloid lesion was 2.70 cm. Patients had at least two lesions. The shape of lesion was mostly linear (Table 2).

Table (2):	Lesions	characteristics	in the	studied	patients
------------	---------	-----------------	--------	---------	----------

All patients (n= 20)		Median (min-max)	Percentage and frequency
Duration of lesion (month)		12.00 (6.00, 25.00)	
Length of lesion (cm)		2.70 (2.10, 4.60)	
Number of lesions	Multiple		11 (55.0%)
	Two		9 (45.0%)
Shape	Linear		10 (50.0%)
	Oval		7 (35.0%)
	Characteristic		3 (15.0%)

Regarding Fitzpatrick skin type, type IV was the most frequent. The most frequent cause of keloids was surgery (Table 3).

Table (3): Skin type and causes of keloid in the studied patients

Skin type	All patients (n= 20)	
III	7 (35.0%)	
IV	10 (50.0%)	
V	3 (15.0%)	
Type of keloid		
Infection	5 (25.0%)	
Surgery	9 (45.0%)	
Trauma	6 (30.0%)	

At each subsequent assessment, both groups showed a significant decline in vascularity, pliability, thickness, and pigmentation, which persisted through the final evaluation. Scar thickness decreased more quickly in the group using fractional CO₂ laser and intralesional triamcinolone; however, the difference between the two groups' rates of thickness reduction was not statistically significant. In both groups, the baseline VSS of the treated areas was considerably higher than that at each subsequent measurements and there was a significantly higher reduction of baseline VSS in fractional CO₂ laser with intralesional triamcinolone group compared to fractional CO₂ laser with intralesional verapamil group at every successive visit (2^{nd} , 3^{rd} , 4^{th}) (Table 4).

Tuble		Verapamil group (n= 20)	Steroid group (n= 20)	Р	
		Median (min-max)	Median (min-max)		
Vascularity	Baseline	1.0 (0.0, 3.0)	1.5 (0.0, 3.0)	0.493	
	First visit	1.0 (0.0, 3.0)	1.0 (0.0, 3.0)*	0.405	
	Second visit	$1.0~(0.0,~2.0)^*$	0.0 (0.0, 2.0)*	0.067	
	Third visit	$0.0~(0.0,~2.0)^{*}$	0.0 (0.0, 1.0)*	0.028	
	Forth visit	$0.0~(0.0,~2.0)^{*}$	0.0 (0.0, 1.0)*	0.009	
	Baseline	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	1.000	
tion	First visit	2.0 (1.0, 2.0)	2.0 (0.0, 2.0)	0.316	
lenta	Second visit	$2.0~(0.0,~2.0)^*$	0.0 (0.0, 2.0)*	0.007	
Pigm	Third visit	$0.0~(0.0,~2.0)^*$	0.0 (0.0, 2.0)*	0.037	
	Forth visit	$0.0~(0.0,~2.0^{*}$	0.0 (0.0, 2.0)*	0.041	
	Baseline	3.0 (1.0, 5.0)	3.0 (1.0, 5.0)	0.754	
ty	First visit	2.0 (0.0, 3.0)*	1.0 (0.0, 3.0)*	0.180	
abili	Second visit	$1.0~(0.0,~2.0)^{*}$	0.0 (0.0, 1.0)*	0.001	
Pli	Third visit	$0.0~(0.0,~2.0)^{*}$	0.0 (0.0, 1.0)*	0.004	
	Forth visit	$0.0~(0.0,~2.0)^{*}$	0.0 (0.0, 1.0)*	0.077	
<u> </u>	Baseline	1.0 (0.0, 3.0)	1.0 (0.0, 3.0)	0.757	
(mm	First visit	$1.0~(0.0,~3.0)^*$	0.0 (0.0, 2.0)*	0.240	
ness	Second visit	$0.0~(0.0,~2.0)^{*}$	0.0 (0.0, 2.0)*	0.289	
hick	Third visit	$0.0~(0.0,~2.0)^{*}$	0.0 (0.0, 1.0)*	0.287	
Γ	Forth visit	$0.0\ {(0.0,\ 2.0)}^{*}$	$0.0\ (0.0,0.0)^{*}$	0.076	
c)	Baseline	6.0 (3.0, 12.0)	7.0 (3.0, 13.0)	0.443	
score	First visit	6.0 (2.0, 10.0)*	5.0 (0.0, 9.0)*	0.103	
DVer	Second visit	4.0 (0.0, 8.0)*	$1.0~(0.0, 7.0)^*$	0.001	
7anco	Third visit	$2.0~(0.0,~8.0)^{*}$	0.0 (0.0, 4.0)*	0.002	
	Forth visit	$2.0~(0.0,~8.0)^*$	0.0 (0.0, 3.0)*	0.003	
* indicates a significant statistical difference between each reading compared to the respective basal value					

Table (4): Comparison of total Vancouver score in studied groups in different visits

There was a significant reduction in both height and surface area of keloid before and after treatment in both fractional CO_2 laser with intralesional verapamil and fractional CO_2 laser with intralesional triamcinolone groups. In comparison to the verapamil group, the fractional CO_2 laser group with intralesional triamcinolone had a considerably greater reduction in lesion height (Table 5).

https://ejhm.journals.ekb.eg/

		Verapamil group (n= 20)	Steroid group (n= 20)	Р	
Height (mm)	Before	2.3 (0.8, 3.9)	2.2 (1.0, 8.8)	0.882	
	After	1.9 (0.6, 3.2)*	0.8 (0.3, 3.4)*	0.003	
Surface area (mm ²)	Before	160.6 (38.9, 934.3)	181.2 (33.6, 806.0)	0.330	
	After	133.3 (37.3, 778.0)*	126.2 (28.0, 315.2)*	0.850	
[*] indicates a significant statistical difference between each reading compared to the basal value					

Table (5): Comparison of scar hieght (mm) and surface area before and after treatment

Fractional CO_2 laser with intralesional verapamil group showed a significant statistical higher occurrence of pain at injection site compared to fractional CO_2 laser with intralesional triamcinolone group.

Regarding patient satisfaction following treatment, there was no statistically significant difference between the fractional CO_2 laser group treated with intralesional verapamil and the fractional CO_2 laser group treated with intralesional triancinolone (Table 6).

Table (6): Side effects at injection site and patient satisfaction after treatment in the studied groups

		Verapamil group (n= 20)	Steroid group (n= 20)	Р	
Pain at injection site	Present	12 (60.0%)	2 (10.0%)	0.001	
	Absent	8 (40%)	18 (90%)		
Post-injection telangiectasia	Present	0 (0.0%)	4 (20.0%)	0.034	
	Absent	20 (100.0%)	16 (80%)	0.034	
	Present	0 (0.0%)	3 (15.0%)	0.072	
Skin atrophy	Absent	20 (100.0%)	17 (85%)		
Patient satisfaction					
Not satisfied and somewhat satisfied (Fair and Poor)		9 (45.0%)	5 (25.0%)	0 185	
Satisfied, very satisfied and extremely satisfied (Good and Excellent)		11 (55.0%)	15 (75.0%)	0.105	

CASE PRESENTATIONS

CASE 1



Before Treatment



After Second Session (After - 8 - Weeks)



After First Session (After - 4 - Weeks)



After Third Session (After - 12 - Weeks)



After Forth Session (After - 16 - Weeks)

Left side (V) = fractional CO₂ laser with intralesional verapamil Right side (S) = fractional CO₂ laser with intralesional triamcinolone

CASE 2



Before Treatment



After First Session (After - 4 - Weeks)



After Second Session (After - 8 - Weeks)



After Third Session (After - 12 - Weeks)



After Forth Session (After - 16 - Weeks)

Left side (V) = fractional CO₂ laser with intralesional verapamil Right side (S) = fractional CO₂ laser with intralesional triamcinolone

DISCUSSION

In the present study, the median age of patients was 22 (min-max=18 - 46) years as this is the age of increase activity and more exposure to trauma. Furthermore, the second to third decade saw the highest prevalence of keloid ⁽¹⁾.

This study included 6 males (30%) and 14 females (70%). The male to female ratio in cohorts of keloids patients is about 1:2, according to a number of earlier research ⁽¹²⁻¹⁵⁾. However, it is generally accepted that both men and women are equally likely to develop keloids, and that patients with keloids who visit the hospital for treatment are more likely to be women due to social factors, such as the fact that women care more about their appearance than men do, are less resistant to medical testing, and are more likely to have their ears pierced⁽¹⁶⁾. **Noishiki** *et al.* ⁽¹⁷⁾ indeed suggests that the female gender possesses a systemic component that is innate and substantially encourages the formation or spread of keloid.

In the current study, family history was present only in 30 % of our patients. This was in accordance with **Aggarwal** *et al.* ⁽¹⁸⁾, **Damanik** *et al.* ⁽¹⁹⁾ **and Khattab and Samir** ⁽²⁰⁾, they found that family history was positive in 17.5%, 37.5% and 43.75 of keloid patients respectively.

In the present study, the shape of keloid was linear, oval and irregular in 10, 7, 3 patients respectively. According to descriptions, keloids can be classified as "regular" with a circular shape and distinct curving lines or "irregular" with asymmetrical shapes and lines ⁽²¹⁾. Furthermore **Bayat** *et al.* ⁽²²⁾ illustrated keloid as (1) geometric (globular, spheroidal, linear, as well as ovoid), (2) recognizable (reniform, petaloid, dumbbell, butterfly, as well as propeller botryoid) and (3) irregular (unrecognizable outlines, nongeometrical).

Regarding Fitzpatrick skin type, we recorded type III, IV, V skin type in 35%, 50%, 15% of patients respectively. This was near similar to another Egyptian study conducted by **Soliman** *et al.*⁽²³⁾ who reported that the most common Fitzpatrick Skin type was type IV in 48.9% of the patients with keloid followed by type III in 46.7% of the patients, while type II was the least common in 4.4% of the patients. The Fitzpatrick skin type has a significant impact on the epidemiology of keloids, with incidences ranging from 4.5 percent to 16 percent in type VI to just 0.09 percent in type I⁽²⁴⁾.

At each subsequent evaluation in the current study, there was a substantial decrease in both groups' vascularity, pliability, thickness, and pigmentation, and this decrease persisted through the final assessment. The fractional CO_2 laser group receiving intralesional triamcinolone showed a faster rate of healing in scar thickness, although this difference in rate of improvement was not statistically significant.

In this study, baseline VSS of treated areas in both groups was noticeably higher than that at each subsequent assessment. Furthermore, there were significantly reduction of baseline VSS in fractional CO_2 laser with intralesional triamcinolone group compared to fractional CO_2 laser with intralesional verapamil group at every successive visits.

In our study, there was a significant reductions in both height and surface area of keloid before and after treatment in both fractional CO_2 laser with intralesional verapamil and fractional CO_2 laser with intralesional triamcinolone groups. The reduction of lesion height was significantly higher in fractional CO_2 laser with intralesional triamcinolone group in comparison with verapamil group.

There are currently many keloid treatment options available, but none of them has yet been shown to be particularly successful⁽²⁵⁾. Interferons, retinoids, botulinum toxin-A, imiquimod 5 percent cream cryotherapy, silicone sheeting, laser therapy, surgical excision, laser therapy intralesional injections of corticosteroids, radiation therapy, compression therapy, 5-fluorouracil, and bleomycin are a few of the modalities that have been tried either alone or in various combinations with varying degrees of success. There are, however, very few attempts to compare their effectiveness and safety⁽¹⁸⁾.

There are few published studies on the topic of treating keloids with a fractionated CO₂ laser and topical triamcinolone acetonide (TAC). In contrast to intralesional often used corticosteroids, the fractionated CO₂ laser enables penetration of topical medications into the dermis after production of a micro-turbine generation simulation system and improves drug delivery to target tissue. Kraeva et al. ⁽⁶⁾, Martin and Collawn ⁽²⁶⁾, and Waibel *et al.* ⁽²⁷⁾ revealed that an African-American man named Fitzgerald VI underwent a reported successful treatment of keloid using a combination therapy of topical TAC ointment and fractionated CO₂ laser, with great cosmetic improvements that lasted 22 months after the procedure. They believed that this combination therapy approach could help individuals with keloids who had skin of color (Fitzpatrick IV–VI) as well as other patients. Following fractionated CO₂ laser treatment, topical TAC ointment use may be an effective, non-invasive substitute for intralesional steroids.

Srivastava *et al.* ⁽²⁸⁾ examined the three regimens of CO_2 laser, triamcinolone, and verapamil for the treatment of keloid growths. At each assessment, all three groups showed a decrease in height, vascularity, pliability, and pigmentation, which persisted until the final evaluation. The measure that remained unaffected by any of the treatment groups was scar pigmentation. Triamcinolone showed a higher rate of improvement in scarring, but there was no statistically significant difference between the three medicines' rates of pigmentation decrease. Each of these therapy modalities had a distinct benefit, and the course of action must be tailored to the specifics of the scar. In contrast to triamcinolone, time is a constraint with laser and verapamil, but they have no negative side effects. Fractional laser therapy should be used on scars. Triamcinolone can be substituted with verapamil, which is more affordable ⁽²⁹⁾.

A common calcium channel antagonist, verapamil hydrochloride increases collagenase while decreasing the production of extracellular matrix components such collagen, glycosaminoglycans, and fibronectin. Early non-randomized clinical trials using intralesional verapamil either alone or as an adjuvant after surgery have demonstrated positive outcomes⁽³⁰⁾.

(29) Ahuia and Chatterjee compared intralesional injections of triamcinolone (40 mg/mL) and/or verapamil (2.5 mg/mL) in a blinded clinical experiment. Up to eight sessions were needed to completely flatten the scar, with injections administered every three weeks. The VSS score was used to assess the scar's pliability, vascularity, height, and color. Regarding scar height, vascularity, and pliability, mean zero VSS scores were attained with both treatments, but the TAC response was quicker and more efficient.

Due to the pharmacological actions of triamcinolone, which reduce proteinase inhibitors, and verapamil, which increase procollagenase secretion, the combination of the two medicines results in an increase in collagenase levels and collagen disintegration within the scar.⁽³¹⁾.

As far as we are aware, this is the first study to examine the effectiveness of utilizing a combination of fractional CO_2 laser and intralesional triamcinolone vs a combination of both fractional CO_2 laser and intralesional verapamil in the treatment of keloids..

In the present study, regarding adverse effects, fractional CO_2 with intralesional verapamil group showed only pain at injection site (60%), While fractional CO_2 laser with intralesional triamcinolone group showed pain at injection site (10%), postinjection telangiectasia (20%) and skin atrophy (15%). Fractional CO_2 laser with intralesional verapamil group showed a significant statistical higher occurrence of pain at injection site compared to fractional CO_2 laser with intralesional triamcinolone group.

In agreement with our result, in **Ahuja and Chatterjee** ⁽²⁹⁾ study, the complication rate was greater in the TAC group (skin atrophy and telangiectasias). On the contrary, verapamil was shown to have no side effects, with the exception of the injection-related pain that required analgesia.

Similarly, **in Srivastava** *et al.* ⁽²⁸⁾ study, after two to three treatment sessions, all three groups had a reduction in discomfort and itch. The majority of patients find telangiectasia, skin shrinkage, and changed pigmentation to be the most common side effects associated with TAC. Regarding patient satisfaction following treatment, there was no statistically significant difference between the fractional CO_2 laser group receiving intralesional verapamil and the fractional CO_2 laser group receiving intralesional triamcinolone.

CONCLUSION

This study revealed that combined fractional CO_2 laser with intralesional triamcinolone therapy showed better clinical improvement compared to combined fractional CO_2 laser with intralesional verapamil therapy, but with more adverse effects.

We postulated that fractional CO_2 laser could increase the depth of penetration of drug applied hence augmenting its effect.

RECOMMENDATIONS

- As it has been demonstrated in numerous research that CO₂ laser is more effective if utilized early, additional large-scale studies with bigger sample sizes are needed to describe the scar's response.
- Larger follow up period is required to assess the maintained response or recurrence.
- Strong recommendations for keloid therapy using fractionated CO₂ laser with TAC injection in patients with skin of color require more randomized controlled trials and split-scar studies to fine-tune fractionated CO₂ laser settings and treatment protocols.
- Further study using different concentration of triamcinolone combined with CO₂ laser to grade against adverse effect as atrophy and telangiectasia.
- It is advised to select a good combination therapy and hold more sessions with more patients in order to achieve better results and greater patient satisfaction.

Conflict of interest: The authors declare no conflict of interest.

Sources of funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution: Authors contributed equally in the study.

REFERENCES

- 1. Thornton N, Garcia B, Hoyer P *et al.* (2021): Keloid scars: an updated review of combination therapies. Cureus, 13(1): e12999. doi: 10.7759/cureus.12999
- 2. Liu H, Wang C, Li C *et al.* (2018): A functional chitosan-based hydrogel as a wound dressing and drug delivery system in the treatment of wound healing. RSC Advances, 8(14): 7533-7549.
- **3.** Jones C, Guiot L, Samy M *et al.* (2015): The use of chemotherapeutics for the treatment of keloid scars. Dermatology Reports, 7(2): 5880. doi: 10.4081/dr.2015.5880.

- 4. Limmer E, Glass D (2020): A Review of current keloid management: mainstay monotherapies and emerging approaches. Dermatology and Therapy, 10(5): 931-948.
- 5. Azzam O, Bassiouny D, El-Hawary M *et al.* (2016): Treatment of hypertrophic scars and keloids by fractional carbon dioxide laser: a clinical, histological, and immunohistochemical study. Lasers in Medical Science, 31(1): 9-18.
- 6. Kraeva E, Ho D, Jagdeo J (2017): Successful treatment of keloid with fractionated carbon dioxide (CO₂) laser and laser-assisted drug delivery of triamcinolone acetonide ointment in an African-American man. Journal of Drugs in Dermatology, 16(9): 925-927.
- 7. Arno A, Gauglitz G, Barret J *et al.* (2014): Up-todate approach to manage keloids and hypertrophic scars: a useful guide. Journal of the International Society for Burn Injuries, 40: (7): 1255-1266.
- 8. Coppola M, Salzillo R, Segreto F *et al.* (2018): Triamcinolone acetonide intralesional injection for the treatment of keloid scars: patient selection and perspectives. Clinical, Cosmetic and Investigational Dermatology, 11: 387-396.
- **9.** Alexandrescu D, Fabi S, Yeh L *et al.* (2016): Comparative results in treatment of keloids with intralesional 5-FU/kenalog, 5-FU/verapamil, enalapril alone, verapamil alone, and laser: A case report and review of the literature. Journal of Drugs in Dermatology, 15(11): 1442-1447.
- **10.** Boggio R, Boggio L, Galvão B *et al.* (2014): Topical verapamil as a scar modulator. Aesthetic Plastic Surgery, 38(5): 968-975.
- **11. Baryza M, Baryza G (1995):** The Vancouver Scar Scale: an administration tool and its interrater reliability. J Burn Care Rehabil., 16: (5): 535-538.
- Attkisson C, Greenfield T (2004): The UCSF Client Satisfaction Scales: I. The Client Satisfaction Questionnaire-8. The use of psychological testing for treatment planning and outcomes assessment: Instruments for adults, Volume 3, 3rd ed. Mahwah, NJ, US: Lawrence Erlbaum Associates Publishers. Pp. 799-811.

file:///C:/Users/Wael/Desktop/helal/UCSFClientSatisfa ctionScales-IAttkissonGreenfield2004.pdf

- **13.** Murray J, Pollack S, Pinnell S (1984): Keloids and hypertrophic scars. Clinics in Dermatology, 2(3): 121-133.
- **14. Ohmori Y (2010):** Analysis of regions where keloids tend to occur. Scar Management, 4: 112-115.
- **15.** Sun L, Wang K, Lee Y (2014): Keloid incidence in Asian people and its comorbidity with other fibrosis-related diseases: a nationwide population-based study. Archives of Dermatological Research, 306(9): 803-808.
- 16. Wang Y, Hunt K, Nazareth I et al. (2013): Do men consult less than women? An analysis of routinely collected UK general practice data. BMJ Open, 3(8): e003320. http://dx.doi.org/10.1136/bmjopen-2013-003320

- 17. Noishiki C, Hayasaka Y, Ogawa R (2019): Sex differences in keloidogenesis: An analysis of 1659 keloid patients in Japan. Dermatology and Therapy, 9(4): 747-754.
- **18.** Aggarwal A, Ravikumar B, Vinay K *et al.* (2018): A comparative study of various modalities in the treatment of keloids. International Journal of Dermatology, 57: (10): 1192-1200.
- **19.** Damanik V, Putra I, Ginting O (2019): Correlation between serum 25-hydroxyvitamin D levels with keloid severity. Open access Macedonian Journal of Medical Sciences, 7(1): 65-67.
- **20.** Khattab F, Samir M (2020): Correlation between serum IL 37 levels with keloid severity. Journal of Cosmetic Dermatology, 19(9): 2428-2431.
- **21.** Akaishi S, Ogawa R, Hyakusoku H (2010): Visual and pathologic analyses of keloid growth patterns. Annals of Plastic Surgery, 64: (1): 80-82.
- 22. Bayat A, Arscott G, Ollier W *et al.* (2004): Description of site-specific morphology of keloid phenotypes in an Afrocaribbean population. British Journal of Plastic Surgery, 57: (2): 122-133.
- **23.** Soliman M, Etman Y, AbdElhameed A *et al.* (2021): Comparative study between Nd-YAG laser, fractional CO₂ laser, and combined Nd-YAG with fractional CO₂ laser in the management of keloid: clinical and molecular study. Journal of Cosmetic Dermatology, 20: (4): 1124-1132.
- 24. Marneros A, Norris J, Olsen B *et al.* (2001): Clinical genetics of familial keloids. Archives of Dermatology, 137(11): 1429-34.
- 25. Ojeh N, Bharatha A, Gaur U *et al.* (2020): Keloids: Current and emerging therapies. Scars, burns & healing, 6: 2059513120940499. doi: 10.1177/2059513120940499.
- 26. Martin M, Collawn S (2013): Combination treatment of CO_2 fractional laser, pulsed dye laser, and triamcinolone acetonide injection for refractory keloid scars on the upper back. Journal of Cosmetic and Laser Therapy, 15(3): 166-170.
- 27. Waibel J, Wulkan A, Rudnick A *et al.* (2019): Treatment of hypertrophic scars using laser-assisted corticosteroid versus laser-assisted 5-fluorouracil delivery. Dermatologic Surgery, 45(3): 423-430.
- **28.** Srivastava S, Kumari H, Singh A (2019): Comparison of fractional CO_2 laser, verapamil, and triamcinolone for the treatment of keloid. Advances in Wound Care, 8(1): 7-13.
- **29.** Ahuja R, Chatterjee P (2014): Comparative efficacy of intralesional verapamil hydrochloride and triamcinolone acetonide in hypertrophic scars and keloids. Burns, 40: (4): 583-588.
- **30.** El-Kamel M, Selim M, Alghobary M (2016): Keloidectomy with core fillet flap and intralesional verapamil injection for recurrent earlobe keloids. Indian Journal of Dermatology Venereology and Leprology, 82: (6): 659-65.
- **31.** Boggio R, Freitas V, Cassiola F *et al.* (2011): Effect of a calcium-channel blocker (verapamil) on the morphology, cytoskeleton and collagenase activity of human skin fibroblasts. Burns, 37: (4): 616-625.