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Fractional co_2 laser with Bleomycin Versus Fractional co_2 Laser with Triamcinolone acetonide in the treatment of Hypertrophic scar and Keloid

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ABSTRACT

Background: Due to deformity, discomfort, and pruritis, hypertrophic scars and keloids are dermal fibro-proliferative illnesses that cause patients to feel misery and have a worse quality of life. They continue to be difficult to manage since there is no approved therapy. Scarring is reduced by fractional co_2 laser without any negative side effects. The treatment of hypertrophic scars and keloids continues to rely heavily on corticosteroids, most often triamcinolone. An anti-cancer drug having an antifibrotic action is bleomycin.

Objective: Comparison between the effectiveness and safety of the combinations of fractional co_2 with bleomycin versus fractional co_2 with triamcinolone in keloids and hypertrophic scar.

Methods: Forty patients were included and split into: group A that included fractional co_2 laser with topical bleomycin and group B included fractional co_2 laser with topical triamcinolone for four sessions with 4 weeks apart. Digital photography, the Vancouver scar scale, and dermoscopy were utilized to assess the effectiveness of the therapy before, after, and three months after each session.

Results: With no discernible variation between the two groups, both medicines significantly increased the total Vancouver, vascularity, and pigmentation ratings of hypertrophic scars and keloids. Both drugs improved pliability score but bleomycin showed better improvement. Both drugs improved height score but triamcinolone showed better improvement. The score improvement was significantly higher in hypertrophic scars than keloids in both groups. Hyperpigmentation was reported in bleomycin. Telangiectasia and hypopigmentation were reported in triamcinolone. By dermoscopy, arborizing, linear and comma shaped vessels have been showed significant improvement in both groups.

Conclusion: Bleomycin should be included among the therapeutic options; it deserves better positioning against keloids and hypertrophic scar. This combination technique offered safe and effective treatment of keloids and hypertrophic scar.

Key Words: Hypertrophic scars; keloids; fractional co_2 laser; bleomycin; triamcinolone

INTRODUCTION

Introduction

Hypertrophic scars and keloids undergo aggressive dermal growth unique to human which result in patients distressing and decreased quality of life due to disfigurement, pain and pruritis **(1)**.

Since there is no widely approved therapy for them, managing them remains difficult. **(2)**.

Scars that are prominent and raised and often regress on their own are referred to as hypertrophic scars. They are often elevated, but seldom rise more than 4 mm above the skin, are red or pink in color, are firm, and itch. These scars also tend to fade over time and do not extend over the basic geographic limits of the incision. **(3)**.

Depending on the original assault, keloids might take the form of solid, slightly painful, fibrous nodules, papules, or plaques. They often have a glossy appearance, are hyperpigmented and erythematous, and include many telangiectasia. They invade the surrounding tissue and go on evolving throughout time without going through a regressive phase. In younger lesions that are experiencing fast development, they are especially related to pruritus and discomfort. Both sexes are equally affected by keloids, albeit young female patients have a greater reported incidence than young male ones. **(4)**.

Burns, severe dermal damage, post-elective surgery, trauma, and keloids may all cause hypertrophic scars and keloids, which can cause deformity and even impair joint mobility. However, keloids can also develop on their own without any prior stimuli. **(5)**.

Keloids and hypertrophic scars affect both sexes equally, with the second decade of life seeing the highest occurrence. **(6)**.

The likelihood of developing keloid scarring may be influenced by certain genetic predispositions. In this situation, those with darker skin tones are more likely than people with lighter complexion to acquire keloid scars. **(7)**.

The Vancouver scar scale, which takes into account vascularity, pigmentation, pliability, and height, is used to evaluate hypertrophic scars and keloids in clinical settings. A reduction in vascularity, pigmentation, and height, as well as a softening of the scar and an improvement in symptoms, will be used to measure the clinical improvements by dermoscopy. **(8)**.

Keloids and hypertrophic scars have several therapy approaches outlined. Conventional therapies include silicone gel sheeting, compressive therapy, topical or intralesional 5-fluorouracil (5-FU), intralesional steroids, surgical excision, cryotherapy, radiation, laser therapy, and photodynamic therapy, among others. **(9)**.

Despite this, no one successful therapy plan has emerged as the gold standard, mostly because of the high rates of keloid recurrence and a lack of thorough studies analyzing the available therapies. Recent developments in the knowledge of disease molecular pathways have ushered in a new age of medication development. **(10)**.

Corticosteroids decrease the volume and height of scars, increase scar pliability, and lessen itchiness and discomfort associated with scars. By suppressing 2-macroglobulin, which in turn inhibits collagenase, the use of corticosteroids prevents the production of collagen and reduces the activity of collagenase. The reduction of endogenous vascular endothelial growth factor (VEGF) caused by steroids is most likely what prevents fibroblasts from proliferating further. The current standard of care is for a monthly intralesional injection of insoluble triamcinolone acetonide (TAC), preferably in conjunction with lidocaine (10–40 mg/ml). **(11)**.

A glycopeptide antibiotic called bleomycin is often used to treat cancer by causing apoptosis and inhibiting collagen production by reducing TGFβ1 activation. It also has an antiviral and antibacterial impact. To prevent toxicity, an injectable bleomycin solution (1.5 IU/ml) at a maximum dosage of 6 ml might be administered by syringe, dermojet, microneedling, or topically after a laser session. **(12)**.

Without causing any noticeable adverse effects, fractional co_2 laser may greatly decrease scarring. Heat stimulates a wound healing response, and the resultant rise in collagen III synthesis may likely cause the texture of the scar to change. Since the light must induce collagen connections strong enough to withstand mild stresses, the heat action of the laser is crucial and must be precisely regulated. **(13)**.

The function of the skin's barrier restricts the absorption of topical products via the epidermis. In the context of a method known as transdermal medication administration, a variety of methods and substances, including microneedling, dermabrasion, radiofrequency, and lasers, have been employed to improve penetration. Due to its ability to create small ablated channels, ablative

fractional lasers are often used in one of these approaches, laser-assisted drug delivery (LADD). The patient, the skin condition and its location, the medicine, and the LADD settings all need to be modified. LADD has been used to treat a variety of disorders, including scars, by combining different topical medicines, such as corticosteroids, photosensitizers, and immunotherapy drugs (imiquimod or 5-fluorouracil). **(14)**.

A white scarring patch with vascular structures against it, including arborizing, are common dermoscopic characteristics of keloids. Linear irregular and comma-shaped veins are also commonly seen. In contrast, the existence of scarring in the form of erythematous or white areas with minimal or nonexistent vascularization is the primary dermoscopic characteristic in hypertrophic scarring. **(15)**.

PATIENTS AND METHODS:

Forty patients who visited the dermatological clinic at Al Zahraa University Hospital in Cairo, Egypt, participated in this comparative research. It was not required to take part in this research. Before enrolling in the research, the included patients were told of its purpose and given their informed permission. The research involving human subjects for the Faculty of Medicine for Girls at Al Azhar University was authorized by the regional ethics committee 2022061376 between September 2020 and September 2021. with the following criteria:

Inclusion criteria

Males or females patients with hypertrophic scar and/or keloid aged from 10 to 50 years old.

Exclusion criteria

Patients receiving other treatment modalities for hypertrophic scar and keloid during and at least 6 months prior to last session, pregnant and lactating females, Photosensitive patients, patients with chronic debilitating diseases, liver, kidney or lung diseases.

METHODS

Every patient was exposed to:

Full history taking

- Information on the patient's name, age, sex, marital status, residence, job, and any unusual behaviors that may be relevant to the patient's care.
- History of current diseases as onset, course, duration, site, number and cause of hypertrophic scar or keloid
- Past history of chronic diseases as diabetes mellitus, hypertension, renal, hepatic, cardiovascular diseases, similar conditions or previous treatment
- Family history of the disease or previous treatment
- History of pregnancy or lactation

Clinical examination

General examination.

Dermatological examination of lesion's site, size and shape and examination utilizing Vancouver scar scale and dermoscopy before and after therapy.

Scar height was accurately measured with calipers where flat scars took score zero (0), scars with height more than zero but less than 2mm took score (1), those with height ranging from 2mm to less than 5mm took score (2) and scars with height of 5mm or more took score (3).

- Scar pliability was evaluated subjectively by palpation if it was felt as normal skin it took score (0), if scar was supple (flexible with minimal resistance) it took score (1), if scar was yielding (giving way to pressure) it took score (2), if scar was firm (rigid, difficult to move, and unyielding to physical pressure) it took score (3), if scar was banding (rope-like tissue that blanches as the scar grows) it took score (4), if there was contracture in the scar (persistent scar shortening that results in deformation or deformity) it took score (5).

Visual examination and the rate of filling after blanching were used to grade the scar's vascularity. If the translucent plastic produced a normal hue that was strikingly similar to the color of the rest of the subject's body (blanching was accomplished), it took score (0), if it gave pink color it took score (1), if it gave red color it took score (2), if it gave purple color it took score (3).

Scar pigmentation was assessed after blanching (Translucent plastic was used to accomplish blanching) and comparing the scar color with the surrounding if it had normal color that closely resembled the color over the rest of one's body it took score (0), if it was hypo pigmented it took score (1), if there was mixed pigmentation it took score (2) if it was hyper pigmented it took score (3) **(16)**.

Investigations

Before starting therapy, testing for the liver and renal function, blood sugar, and total blood count was performed.

Dermoscopic evaluation

In keloids, arborizing, linear irregular, and comma-shaped vessels are commonly seen against a backdrop of a white scarring area. In contrast, the existence of scarring in the form of erythematous or white areas with minimal or nonexistent vascularization is the primary dermoscopic characteristic in hypertrophic scarring**(17)**.

Treatment

Patients were split into two equal groups:

- **Group A:** had 10 patients with hypertrophic scars and 10 with keloids. They received combination of fractional CO_2 laser followed by topical bleomycin.
- **Group B:** comprised 10 patients with keloids and 10 patients with hypertrophic scars. They got a mix of topical triamcinolone acetenoid and fractional co_2 laser treatment.
- 60 minutes prior the laser session, a topical anesthetic cream (lidocaine 25% or pridocaine 25%) was placed under occlusion and removed shortly before.
- Each patient in both groups had four fractional co_2 laser treatments, spaced four weeks apart, with the following settings:
  - **Hypertrophic scars**: Smart stack, 25 W, stack 3, 600 μs of dwell duration, 700 μm for skin type III, and 800 μm for skin type IV spacing.
  - **Keloids:** Smart stack, 30 W, stack 4, 1000-μs living duration, and 800-μm spacing are used, then triamcinolone acetonide and bleomycin are applied topically.
  - After application of fractional co_2 laser, we applied topical bleomycin in group (A).A solution of 0.1 mL /cm^2 bleomycin (1.5 IU/mL) in each lesion apart at intervals of four weeks with a maximum of 6 mL per session, until favorable aesthetic results and symptom reduction. Bleomycin diluted in normal saline and when kept at 4 °C, kept stable and efficient for up to 7 months. **(18)**.
  - After application of fractional co_2 laser, we applied topical triamcinolone acetonide in group (B). The size, location, and patient's age all affected how much triamcinolone acetonide was present. Triamcinolone acetonide was often used at a dosage of 10–20 mg/ml when diluted in normal saline, while it might be administered at a dosage of 40 mg/ml for a challenging, bulky lesion. Every four weeks, sessions were repeated once. The severity of the lesion, treatment response, and potential adverse effects all influence the overall number of sessions. **(19)**.

Assessment of the clinical response

Digital photographs, the Vancouver Scar Scale score, and dermoscopy were used to assess the effectiveness of treating hypertrophic scars and keloids after fractional co_2 laser treatment and topical usage of bleomycin in group (A) or triamcinolone acetonide in group (B). These assessments were made at the baseline, each session, and after three months of follow-up.

The score's declining value suggested that the scar's clinical condition had improved, where the change in value of different parameters (Scar elasticity, height, vascularity, and color) together with the total score was statistically tested to evaluate whether the change was statistically significant, highly significant or non-significant **(20).** This improvement was expressed qualitatively as:

(0-10%) = no improvement (GO).
(11-25%) = Poor improvement (GI).
(26-50%) = Fair improvement (G2).
(51-75%) = Good improvement (G3).
(76-100%) = Excellent improvement (G4).

Patient satisfaction scale

At their last appointment, patients were asked to score their level of satisfaction overall, indicating whether they were not pleased, somewhat satisfied, satisfied, or extremely satisfied, utilizing the following grades:

Grade I = not satisfied
Grade II = slightly satisfied
Grade III = satisfied
Grade IV = very satisfied

Safety assessment

Other problems such as erythema, discomfort, ulceration, burning sensation, ecchymosis, infection, post-inflammatory hypo or hyperpigmentation, and any allergy signs were explained to the patients.

Follow up assessment after treatment

Following the conclusion of therapy session, the patients were observed monthly for three months to look for any signs of recurrence, complications, or worsening of the lesions.

RESULTS

Table 1: Comparison of the demographics and clinical features of the two study groups

Demographics and clinical characteristics		Group A No.= 20	Group B No.= 20	Test value	P- value	Sig.
Age	Mean±SD	21.90 ± 10.99	25.95 ± 14.83	-0.981•	0.333	NS
	Range	10 – 49	10 – 50			
Sex	Males	13 (65.0%)	10 (50.0%)	0.921*	0.337	NS
	Females	7 (35.0%)	10 (50.0%)			
Duration (years)	Mean±SD	2.35 ± 1.93	3.00 ± 2.58	-0.904•	0.372	NS
	Range	1 – 9	1 – 10			
Lesion	Hypertrophic scar	10 (50.0%)	10 (50.0%)	0.000*	1.000	NS
	Keloid	10 (50.0%)	10 (50.0%)			
Etiology	Surgery	11 (55.0%)	9 (45.0%)	1.176*	0.882	NS
	Burn	3 (15.0%)	5 (25.0%)			
	Post infection	3 (15.0%)	4 (20.0%)			
	Trauma	2 (10.0%)	1 (5.0%)			
	Spontaneous	1 (5.0%)	1 (5.0%)			
Site	Pre sternal	2 (10.0%)	5 (25.0%)	5.286*	0.382	NS
	Extremities	12 (60.0%)	8 (40.0%)			
	Face	2 (10.0%)	3 (15.0%)			
	Neck	1 (5.0%)	1 (5.0%)			
	Back	3 (15.0%)	1 (5.0%)			
	Abdomen	0 (0.0%)	2 (10.0%)			
Skin type	III	11 (55.0%)	8 (40.0%)	1.029*	0.598	NS
	IV	8 (40.0%)	10 (50.0%)			
	V	1 (5.0%)	2 (10.0%)			
Family history	Negative	14 (70.0%)	17 (85.0%)	1.290*	0.256	NS
	Positive	6 (30.0%)	3 (15.0%)			
Smoking	Negative	17 (85.0%)	20 (100.0%)	3.243*	0.072	NS
	Positive	3 (15.0%)	0 (0.0%)			
Number of lesions	Single	14 (70.0%)	12 (60.0%)	1.154*	0.562	NS
	Two	1 (5.0%)	3 (15.0%)			
	Multiple	5 (25.0%)	5 (25.0%)			

Table 2: Comparison of the pretreatment Vancouver scar scale scores of the two investigated groups

Before		Group A No.= 20	Group B No.= 20	Test value≠	P- value	Sig.
Total VSSS	**Median (IQR)**	8 (6 – 11)	9 (6 – 11)	-0.398	0.691	NS
	Mean±SD	7.80 ± 2.75	8.05 ± 2.78			
	Range	4 – 12	2 – 12			
Vascularity	**Median (IQR)**	1 (1 – 2)	2 (1 – 2)	-0.725	0.468	NS
	Mean±SD	1.30 ± 0.98	1.45 ± 0.89			
	Range	0 – 3	0 – 3			
Pigmentation	**Median (IQR)**	2 (0.5 – 3)	2 (0 – 2.5)	-0.157	0.875	NS
	Mean±SD	1.70 ± 1.17	1.65 ± 1.18			
	Range	0 – 3	0 – 3			
Pliability	**Median (IQR)**	3 (2 – 4)	3 (3 – 4)	-0.589	0.556	NS
	Mean±SD	2.95 ± 0.83	3.10 ± 0.91			
	Range	2 – 4	1 – 5			
Height	**Median (IQR)**	2 (2 – 2)	2 (1.5 – 2)	-0.328	0.743	NS

	Mean±SD	2.05 ± 1.05	1.85 ± 0.59			
	Range	1 – 6	1 – 3			

Table 3: Comparison of the Vancouver scar scale scores of the two investigated groups after treatment

After		**Group A**	**Group B**	**Test value≠**	**P- value**	**Sig.**
		No.= 20	**No.= 20**			
Total VSSS	**Median (IQR)**	3.5 (1 – 5.5)	3 (2 – 4)	-0.341	0.733	NS
	Mean±SD	3.65 ± 2.85	3.30 ± 2.45			
	Range	0 – 9	0 – 11			
Vascularity	**Median (IQR)**	1 (0 – 1)	1 (0.5 – 1)	-0.560	0.576	NS
	Mean±SD	0.80 ± 0.83	0.85 ± 0.59			
	Range	0 – 3	0 – 2			
Pigmentation	**Median (IQR)**	1 (0 – 2)	0 (0 – 2)	-1.175	0.240	NS
	Mean±SD	1.15 ± 1.18	0.75 ± 1.07			
	Range	0 – 3	0 – 3			
Pliability	**Median (IQR)**	0.5 (0 – 1.5)	1.5 (1 – 3.5)	-2.245	0.025	S
	Mean±SD	0.85 ± 1.04	1.85 ± 1.5			
	Range	0 – 3	0 – 4			
Height	**Median (IQR)**	1 (0 – 1.5)	0 (0 – 1)	-2.082	0.037	S
	Mean±SD	0.85 ± 0.81	0.35 ± 0.59			
	Range	0 – 2	0 – 2			

Table 4: Vancouver scar scale score before and after treatment in group A

Group A		**Before**	**After**	**Test value≠**	**P- value**	**Sig.**
Total VSSS	**Median (IQR)**	8 (6 – 11)	3.5 (1 – 5.5)	-3.937	0.000	HS
	Mean±SD	7.80 ± 2.75	3.65 ± 2.85			
	Range	4 – 12	0 – 9			
Vascularity	**Median (IQR)**	1 (1 – 2)	1 (0 – 1)	-2.714	0.007	HS
	Mean±SD	1.30 ± 0.98	0.80 ± 0.83			
	Range	0 – 3	0 – 3			
Pigmentation	**Median (IQR)**	2 (0.5 – 3)	1 (0 – 2)	-2.495	0.013	S
	Mean±SD	1.70 ± 1.17	1.15 ± 1.18			
	Range	0 – 3	0 – 3			
Pliability	**Median (IQR)**	3 (2 – 4)	0.5 (0 – 1.5)	-4.005	0.000	HS
	Mean±SD	2.95 ± 0.83	0.85 ± 1.04			
	Range	2 – 4	0 – 3			
Height	**Median (IQR)**	2 (2 – 2)	1 (0 – 1.5)	-3.235	0.001	HS
	Mean±SD	2.05 ± 1.05	0.85 ± 0.81			
	Range	1 – 6	0 – 2			

Table 5: Vancouver scar scale score before and after treatment in group B

Group B		**Before**	**After**	**Test value≠**	**P- value**	**Sig.**
Total VSSS	**Median (IQR)**	9 (6 – 11)	3 (2 – 4)	-3.831	0.000	HS
	Mean±SD	8.05 ± 2.78	3.30±2.45			
	Range	2 – 12	0 – 11			
Vascularity	**Median (IQR)**	2 (1 – 2)	1 (0.5 – 1)	-2.972	0.003	HS
	Mean±SD	1.45 ± 0.89	0.85 ± 0.59			
	Range	0 – 3	0 – 2			

Pigmentation	**Median (IQR)**	2 (0 – 2.5)	0 (0 – 2)	-2.877	0.004	HS
	Mean±SD	1.65 ± 1.18	0.75 ± 1.07			
	Range	0 – 3	0 – 3			
Pliability	**Median (IQR)**	3 (3 – 4)	1.5 (1 – 3.5)	-2.751	0.006	HS
	Mean±SD	3.10 ± 0.91	1.85 ± 1.5			
	Range	1 – 5	0 – 4			
Height	**Median (IQR)**	2 (1.5 – 2)	0 (0 – 1)	-3.827	0.000	HS
	Mean±SD	1.85 ± 0.59	0.35 ± 0.59			
	Range	1 – 3	0 – 2			

Table 6: Comparison of the overall Vancouver scar scale score before and after therapy for the two investigated groups

Total VSSS		**Group A**	**Group B**	**Test value≠**	**P- value**	**Sig.**
		No.= 20	**No.= 20**			
Before	**Median (IQR)**	8 (6 – 11)	9 (6 – 11)	-0.398	0.691	NS
	Mean±SD	7.80 ± 2.75	8.05 ± 2.78			
	Range	4 – 12	2 - 12			
After	**Median (IQR)**	3.5 (1 – 5.5)	3 (2 – 4)	-0.341	0.733	NS
	Mean±SD	3.65 ± 2.85	3.30 ± 2.45			
	Range	0 - 9	0 - 11			

Table 7: Comparison between the two study groups as regard vascularity before and after treatment

Vascularity		**Group A**	**Group B**	**Test value≠**	**P- value**	**Sig.**
		No.= 20	**No.= 20**			
Before	**Median (IQR)**	1 (1 – 2)	2 (1 – 2)	-0.725	0.468	NS
	Mean±SD	1.30 ± 0.98	1.45 ± 0.89			
	Range	0 – 3	0 - 3			
After	**Median (IQR)**	1 (0 – 1)	1 (0.5 – 1)	-0.560	0.576	NS
	Mean±SD	0.80 ± 0.83	0.85 ± 0.59			
	Range	0 - 3	0 - 2			

Table 8: Comparison of the pigmentation of the two examined groups before and after treatment

Pigmentation		**Group A**	**Group B**	**Test value≠**	**P- value**	**Sig.**
		No.= 20	**No.= 20**			
Before	**Median (IQR)**	2 (0.5 – 3)	2 (0 – 2.5)	-0.157	0.875	NS
	Mean±SD	1.70 ± 1.17	1.65 ± 1.18			
	Range	0 – 3	0 - 3			
After	**Median (IQR)**	1 (0 – 2)	0 (0 – 2)	-1.175	0.240	NS
	Mean±SD	1.15 ± 1.18	0.75 ± 1.07			
	Range	0 - 3	0 - 3			

Table 9: Comparison between the two study groups as regard pliability before and after treatment

Pliability		**Group A**	**Group B**	**Test value≠**	**P- value**	**Sig.**
		No.= 20	**No.= 20**			
Before	**Median (IQR)**	3 (2 – 4)	3 (3 – 4)	-0.589	0.556	NS
	Mean±SD	2.95 ± 0.83	3.10 ± 0.91			
	Range	2-4	1 – 5			
After	**Median (IQR)**	0.5 (0 – 1.5)	1.5 (1 – 3.5)	-2.245	0.025	S
	Mean±SD	0.85 ± 1.04	1.85 ± 1.5			
	Range	0 - 3	0 – 4			

Table 10: Comparison between the two study groups as regard Height before and after treatment

Height	**Group A**	**Group B**	**Test value≠**	**P- value**	**Sig.**

		No.= 20	No.= 20			
Before	**Median (IQR)** **Mean±SD** **Range**	2 (2 – 2) 2.05 ± 1.05 1 – 6	2 (1.5 – 2) 1.85 ± 0.59 1 – 3	-0.328	0.743	NS
After	**Median (IQR)** **Mean±SD** **Range**	1 (0 – 1.5) 0.85 ± 0.81 0 - 2	0 (0 – 1) 0.35 ± 0.59 0 – 2	-2.082	0.037	S

Table 11: Comparison of change in Vancouver scar scale score between the two studied groups

% of Change		Group A	Group B	Test value≠	P- value	Sig.
		No.= 20	No.= 20			
Total VSSS	**Median (IQR)**	52.27 (36.93 – 83.33)	63.64 (39.61 – 77.27)	-0.027	0.978	NS
	Range	14.29 – 100	0 – 100			
Vascularity	**Median (IQR)**	16.67 (0 – 75)	50 (0 – 50)	-0.242	0.809	NS
	Range	0 – 100	0 – 100			
Pigmentation	**Median (IQR)**	33.33 (0 – 100)	66.67 (0 – 100)	-0.791	0.429	NS
	Range	0 – 100	0 – 100			
Pliability	**Median (IQR)**	83.33 (50 – 100)	50 (26.65 – 70.83)	-2.065	0.039	S
	Range	25 – 100	0 – 100			
Height	**Median (IQR)**	50 (0 – 100)	100 (66.67 – 100)	-1.961	0.050	NS
	Range	0 – 100	0 – 100			

Table 12: Comparison of side effects between the two studied groups

Side effect	Group A	Group B	Test value*	P- value	Sig.
	No.= 20	No.= 20			
Hyper pigmentation	2 (10.0%)	0 (0.0%)	2.105	0.147	NS
Telangectasia	0 (0.0%)	2 (10.0%)	2.105	0.147	NS
Hypo pigmentation	0 (0.0%)	2 (10.0%)	2.105	0.147	NS

Table 13: Patient satisfaction between two studied groups

Patient satisfaction	Group A		Group B		Test value*	P- value	Sig.
	No.	%	No.	%			
Grade I (no satisfied)	2	10.0%	1	5.0%	0.360	0.549	NS
Grade II (slightly Satisfied)	6	30.0%	5	25.0%	0.125	0.724	NS
Grade III (satisfied)	5	25.0%	6	30.0%	0.125	0.724	NS
Grade IV (very satisfied)	7	35.0%	8	40.0%	0.107	0.744	NS

Table 14: Clinical response (Improvement) between two studied groups and its grading using five point scale

Clinical response (Improvement)	Group A		Group B		Test value*	P-value	Sig.
	No.	%	No.	%			
Grade 0 (No improvement) (0-10%)	0	0.0%	2	10.0%	2.105	0.147	NS
Grade 1 (Poor improvement) (11-25%)	2	10.0%	1	5.0%	0.360	0.549	NS
Grade 2 (Fair improvement) (26-50%)	8	40.0%	6	30.0%	0.440	0.507	NS
Grade 3 (Good improvement) (51-75%)	3	15.0%	6	30.0%	1.290	0.256	NS
Grade 4 (Excellent improvement) (>75%)	7	35.0%	5	25.0%	0.476	0.490	NS

Table 15: Comparison between HTS and keloid in Vancouver scar scale before and after treatment in group A

Group A	Hypertrophic scar	P1	Keloid	P2

		Before	After		Before	After	
Total VSSS	**Mean ± SD**	5.60 ± 1.65	2 ± 2	0.005 (HS)	10 ± 1.56	5.3 ± 2.67	0.005(HS)
	Median (IQR)	6 (4 – 6)	1.5 (1 – 2)		11 (8 – 11)	5 (5 – 7)	
	Range	4 – 9	0 – 6		8 – 12	1 – 9	
Vascularity	**Mean ± SD**	2 ± 0.82	1.3 ± 0 82	0.034(S)	0.6 ± 0.52	0.3 ± 0.48	0.083(NS)
	Median (IQR)	2 (1 – 3)	1 (1 – 2)		1 (0 – 1)	0 (0– 1)	
	Range	1 – 3	0 – 3		0 – 1	0 – 1	
Pigmentation	**Mean ± SD**	0.9 ± 1.1	0.3 ± 0.67	0.084(NS)	2.5 ± 0.53	2 ± 0.94	0.059(NS)
	Median (IQR)	0.5 (0 – 2)	0 (0 – 0)		2.5 (2 – 3)	2 (2 – 3)	
	Range	0 – 3	0 – 2		2 – 3	0 – 3	
Pliability	**Mean ± SD**	2.5 ± 0.71	0.6 ± 0.97	0.004(HS)	3.4 ± 0.7	1.1 ± 1.1	0.004(HS)
	Median (IQR)	2 (2 – 3)	0 (0 – 1)		3.5 (3 – 4)	1 (0 – 2)	
	Range	2 – 4	0 – 3		2 – 4	0 – 3	
Height	**Mean ± SD**	2 ± 1.49	0.8 ± 0.79	0.026(S)	2.1 ± 0.32	0.9 ± 0.88	0.016(S)
	Median (IQR)	2 (1 – 2)	1 (0 – 1)		2 (2 – 2)	1 (0 – 2)	
	Range	1 – 6	0 – 2		2 – 3	0 – 2	

Table 16: Comparison between HTS and keloid in Vancouver scar scale before and after treatment in group B

Group B		**Hypertrophic scar**		**P1**	**Keloid**		**P2**
		Before	**After**		**Before**	**After**	
Total VSSS	**Mean ± SD**	7.4 ± 3.13	2.1 ± 1.52	0.007(HS)	8.7 ± 2.36	4.5 ± 2.68	0.005(HS)
	Median (IQR)	9 (5 – 9)	2.5 (1 – 3)		8 (7 – 11)	3.5 (3 – 5)	
	Range	2 – 11	0 – 4		6 – 12	2 – 11	
Vascularity	**Mean ± SD**	1.2 ± 1.03	0.6 ± 0.52	0.014(S)	1.7 ± 0.67	1.1 ± 0.57	0.063(NS)
	Median (IQR)	2 (0 – 2)	1 (0 – 1)		2 (1 – 2)	1 (1 – 1)	
	Range	0 – 2	0 – 1		1 – 3	0 – 2	
Pigmentation	**Mean ± SD**	1.6 ± 0.84	0.4 ± 0.84	0.014(S)	1.7 ± 1.49	1.1 ± 1.2	0.059(NS)
	Median (IQR)	2 (2 – 2)	0 (0 – 0)		2.5 (0 – 3)	1 (0 – 2)	
	Range	0 – 2	0 – 2		0 – 3	0 – 3	
Pliability	**Mean ± SD**	3.5 ± 0.71	1.5 ± 1.08	0.004 (HS)	2.7 ± 0.95	2.2 ±1.81	0.339(NS)
	Median (IQR)	3 (3 – 4)	1 (1 – 2)		3 (2 – 3)	2.5 (0 – 4)	

	Range	3 – 5	0 – 4		1 – 4	0 – 4	
Height	**Mean ± SD**	1.9 ± 0.74	0.5 ± 0.71	0.008(HS)	1.8 ± 0.42	0.2 ± 0.42	0.005(HS)
	Median (IQR)	2 (1 – 2)	0 (0 – 1)		2 (2 – 2)	0 (0 – 0)	
	Range	1 – 3	0 – 2		1 – 2	0 – 1	

Table 17: Relation between dermoscopic changes and Vancouver scar scale score before and after treatment in group A

Group A		**Total VSSS**		**Test value**	**P-value**	**Sig.**
		Median(IQR)	**Range**			
Before						
Arborizing vessels	**Absent**	52.27 (40.97 – 75.00)	25.00 – 83.33	3.588‡‡	0.310	NS
	+	83.33 (54.55 – 100.00)	54.55 – 100.00			
	++	62.63 (36.36 – 94.44)	36.36 – 100.00			
	+++	37.50 (27.27 – 50.00)	14.29 – 87.50			
linear vessels	**Absent**	60.61 (52.27 – 75.00)	50.00 – 83.33	1.918‡‡	0.383	NS
	+	37.50 (36.36 – 44.44)	36.36 – 44.44			
	++	54.55 (36.36 – 87.50)	14.29 – 100.00			
comma shaped vessels	**Absent**	50.00 (37.50 – 83.33)	14.29 – 100.00	-0.372‡	0.710	NS
	+	83.33 (25.00 – 88.89)	25.00 – 88.89			
After						
Arborizing vessels	**Absent**	52.27 (36.93 – 83.33)	14.29 – 100.00	-0.806‡	0.420	NS
	+	68.75 (43.18 – 93.75)	36.36 – 100.00			
linear vessels	**Absent**	47.22 (36.93 – 60.61)	25.00 – 83.33	1.561‡‡	0.458	NS
	+	54.55 (37.50 – 83.33)	14.29 – 100.00			
	++	88.89 (27.27 – 100.00)	27.27 – 100.00			

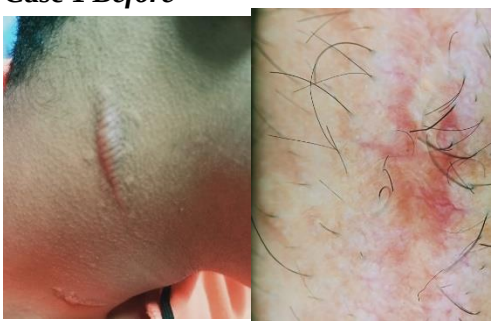
Table 18: Relation between dermoscopic changes and Vancouver scar scale score before and after treatment in group B

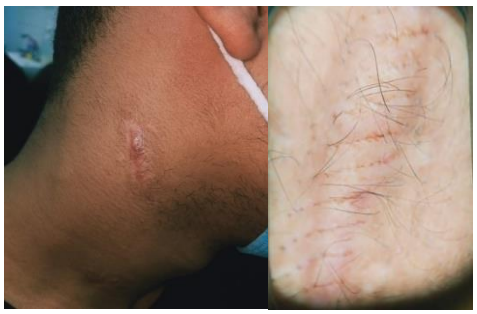
Group B		**Total VSSS**		**Test value**	**P-value**	**Sig.**
		Median(IQR)	**Range**			
Before						
Arborizing vessels	**Absent**	66.67 (42.86 – 88.89)	0.00 – 100.00	1.649‡‡	0.648	NS
	+	61.36 (50.00 – 72.73)	50.00 – 72.73			
	++	65.15 (63.64 – 66.67)	63.64 – 66.67			
	+++	39.61 (28.57 – 63.64)	8.33 – 100.00			
linear vessels	**Absent**	53.41 (12.50 – 90.91)	0.00 – 100.00	0.135‡‡	0.935	NS
	+	65.15 (63.64 – 66.67)	63.64 – 66.67			
	++	56.82 (42.86 – 72.73)	8.33 – 100.00			
comma shaped vessels	**Absent**	63.64 (42.86 – 72.73)	0.00 – 100.00	-0.106‡	0.915	NS
	+	66.67 (8.33 – 88.89)	8.33 – 88.89			
After						
Arborizing vessels	**Absent**	66.67 (42.86 – 81.82)	0.00 – 100.00	2.569‡‡	0.463	NS
	+	50.00 (42.86 – 63.64)	36.36 – 88.89			
	++	63.64 (63.64 – 63.64)	63.64 – 63.64			
	+++	8.33 (8.33 – 8.33)	8.33 – 8.33			
linear vessels	**Absent**	63.64 (37.50 – 66.67)	0.00 – 72.73	0.649‡‡	0.723	NS
	+	65.91 (35.71 – 94.44)	8.33 – 100.00			
	++	54.76 (39.61 – 77.78)	36.36 – 88.89			

Illustrative Cases:

Examples of patients in group (A):

Case 1 ***Before*** ***After***





Male patient, 18 years old with hypertrophic scar on right side of neck of 2 years duration occurred after trauma.

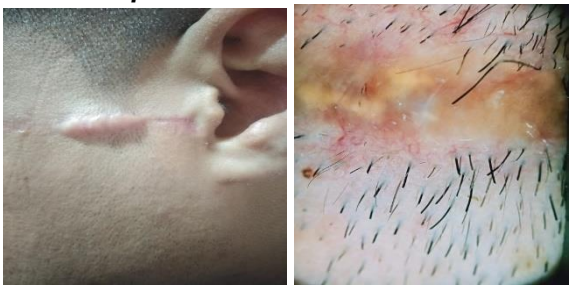
Vss was 9 out of 14 before treatment and became 4 out of 14 after treatment.

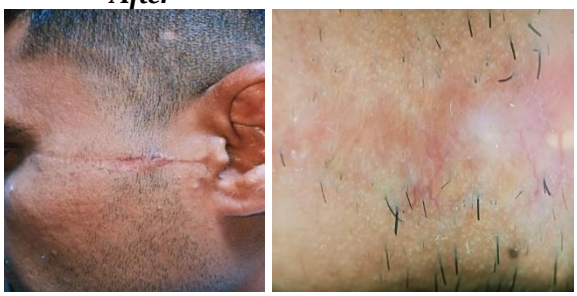
Marked improvement in pliability and vascularity.

Dermoscopic picture of hypertrophic scar shows linear blood vessels before treatment which partially disappeared after treatment and comma shaped vessels which markedly disappeared after treatment.

Case 2

Before ***After***





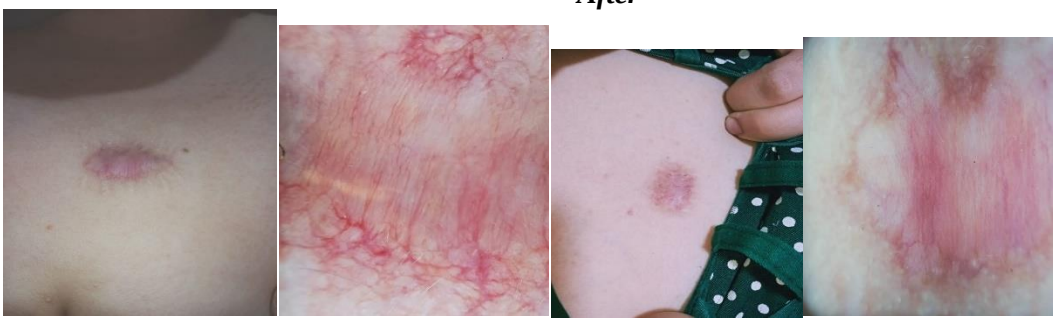
Male patient, 24 years old with hypertrophic scar on left side of face of 1 year duration occurred after trauma.

Vss was 6 out of 14 before treatment and became 1 out of 14 after treatment with complete scar flattening.

Dermoscopic picture of hypertrophic scar shows linear blood vessels before treatment which partially disappeared after treatment.

Case 3

Before ***After***



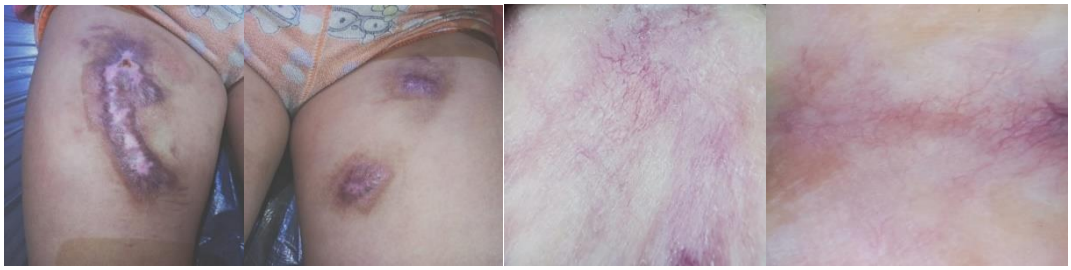
Female patient, 29 years old with spontaneous keloid on front of chest of 1 year duration.

Vss was 8 out of 14 before treatment and became 1 out of 14 after treatment with complete scar flattening.

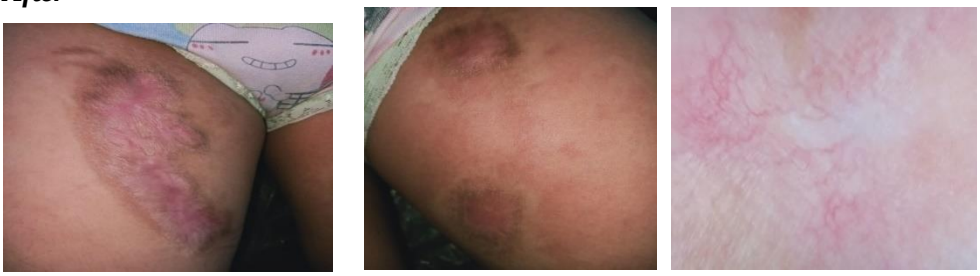
Dermoscopic picture of keloid shows arborizing and linear blood vessels before treatment which partially disappeared after treatment.

Case 4

Before



After



Female patient, 11 years old with multiple keloids on front of right and left sides of thigh of 2 years duration.

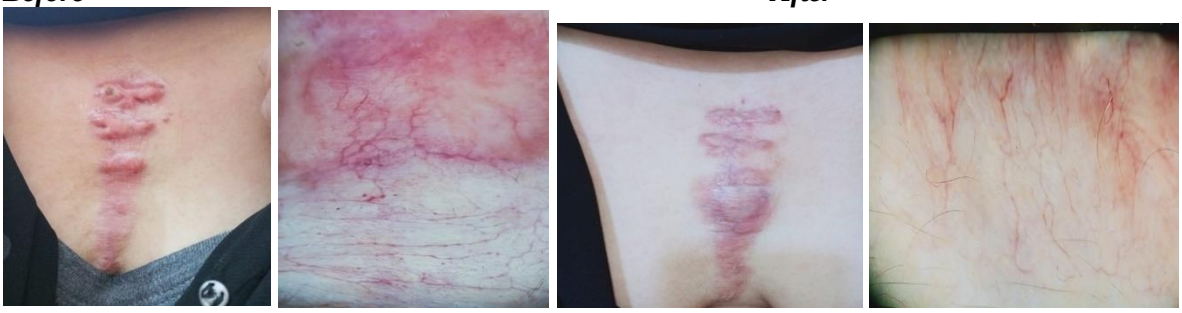
Vss was 12 out of 14 before treatment and became 5 out of 14 after treatment.

Marked improvement in height, pliability and pigmentation.

Dermoscopic picture of keloid shows arborizing and linear blood vessels before treatment which partially disappeared after treatment.

Case 5

Before ***After***



Female patient, 49 years old with multiple keloids on front of chest of 5 year duration occurred after open heart surgery.

The patient was steroid non responder as she reported previous 5 intralesional injection of triamcinolone with no response 2years ago.

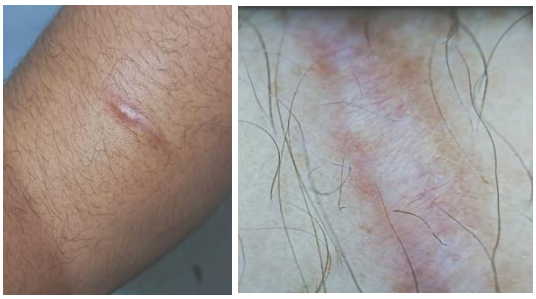
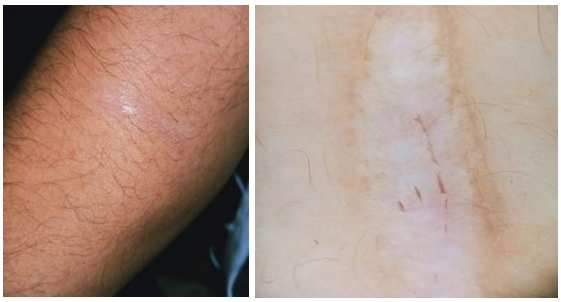
Vss was 11 out of 14 before treatment and became 5 out of 14 after treatment with complete scar flattening.

Dermoscopic picture of keloid shows arborizing and linear blood vessels before treatment which partially disappeared after treatment.

Examples of patients in group (B):

Case 6

Before ***After***

Male patient, 20 years old with hypertrophic scar on extensor surface of right forearm of 2 years duration which occurred after trauma (cut wound).

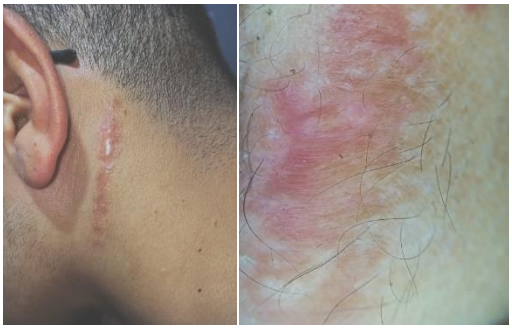
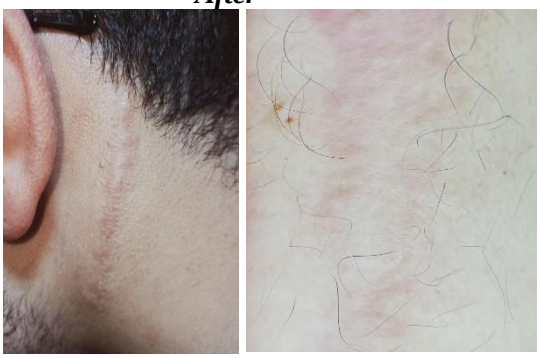
Vss was 6 out of 14 before treatment and became 1 out of 14 after treatment.

Marked improvement in height, vascularity and pigmentation.

Dermoscopic picture of hypertrophic scar shows linear blood vessels before treatment which completely disappeared after treatment.

Case 7

Before ***After***

Male patient, 24 years old with hypertrophic scar behind the left ear of 1 years duration which occurred after trauma (cut wound).

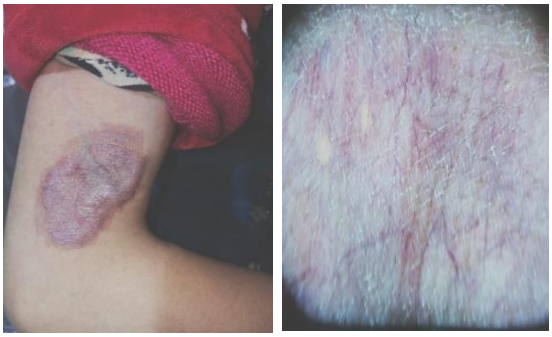
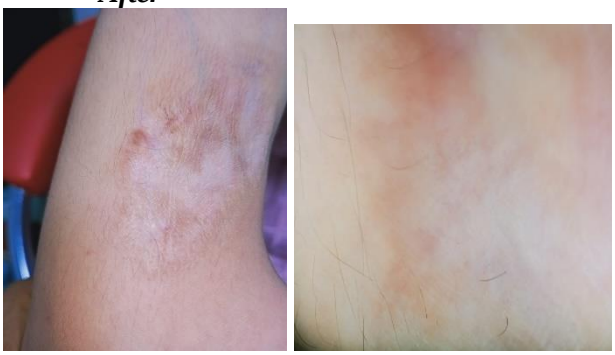
Vss was 7 out of 14 before treatment and became 1 out of 14 after treatment.

Marked improvement in height, pliability and vascularity.

Dermoscopic picture of hypertrophic scar shows comma shaped vessels before treatment which completely disappeared after treatment.

Case 8

Before ***After***

Female patient, 10 years old with keloid on right arm of 1 year duration.

Vss was 9 out of 14 before treatment and became 1 out of 14 after treatment.

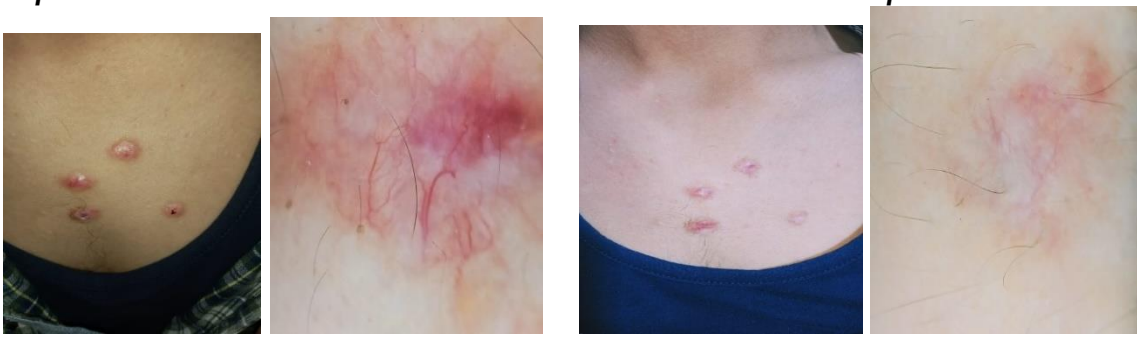
Marked improvement in height, pliability and vascularity.

Hypopigmentation is a side effect.

Dermoscopic picture of keloid shows arborizing and linear blood vessels before treatment which completely disappeared after treatment.

Case 9

Before ***After***



Male patient, 21 years old with multiple keloids on front of chest of 1 year duration which occurred after folliculitis.

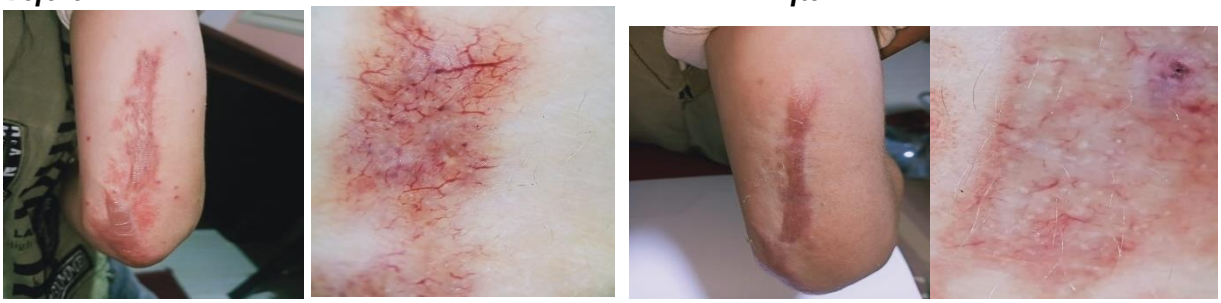
Vss was 7 out of 14 before treatment and became 5 out of 14 after treatment.

Marked improvement in height, pliability and vascularity.

Dermoscopic picture of keloid shows arborizing and linear blood vessels before treatment which partially disappeared after treatment.

Case 10

Before ***After***



Male patient, 10 years old with hypertrophic scar on right arm of 5 months duration.

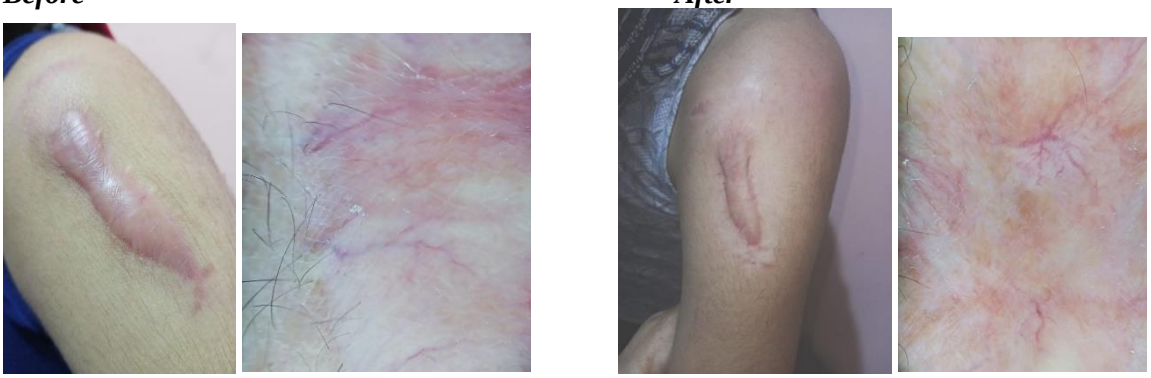
Vss was 9 out of 14 before treatment and became 5 out of 14 after treatment.

Marked improvement in height, pliability and vascularity.

Dermoscopic picture of keloid shows arborizing and linear blood vessels before treatment which partially disappeared after treatment.

Case 11

Before ***After***

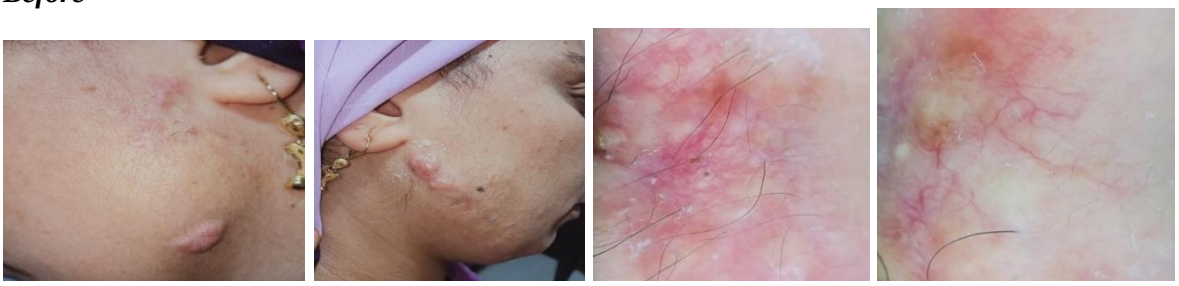


Male patient, 13 years old with hypertrophic scar on left arm of 3 years duration which occurred after trauma.

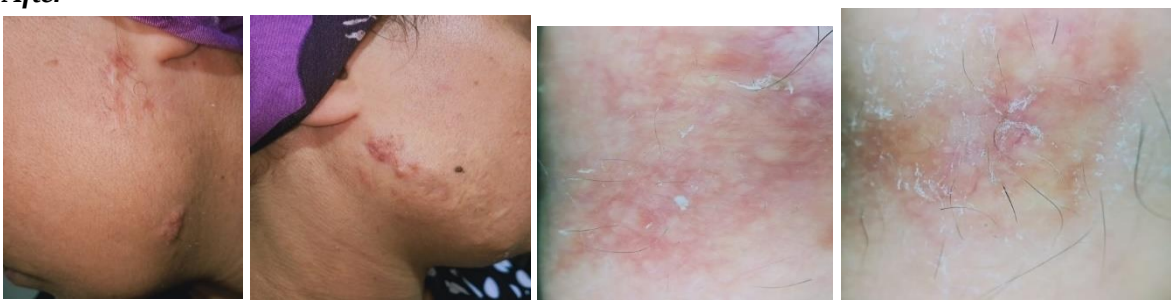
Vsss was 11 out of 14 before treatment and became 4 out of 14 after treatment.
Mild improvement in height, pliability.
Dermoscopic picture of hypertrophic scar shows arborizing and linear blood vessels before treatment which partially disappeared after treatment.

Case 12

Before



After



Female patient, 46 years old with multiple keloids on right and left sides of face of 2 years duration which occurred after folliculitis.
The patient was reported previous 4 intralesional injection of unknown subsctance with no response 4years ago.
Vss was 8 out of 14 before treatment and became 4 out of 14 after treatment
Marked improvement in height and pliability.
Dermoscopic picture of keloid shows arborizing, linear and comma shaped blood vessels before treatment, which arborizing vessels completely disappeared and linear vessels partially disappeared after treatment.

DISCUSSION

Keloids and hypertrophic scars are fibrotic disorders with overproduction of extracellular matrix and noticeable fibroblast proliferation that serve as models for altered wound healing. Their precise pathophysiology and etiology are still poorly known. There is no one treatment option that works best for all keloids and hypertrophic scars. **(21)**.
Fractional co_2 laser can significantly reduce scarring without notable side effects through inducing a wound healing response with heat and subsequent increase in collagen III production **(22)**.
Corticosteroids are recognized as the first-line drugs for hypertrophic scars and keloids through suppressing the proliferation of fibroblasts through suppressing the level of endogenous VEGF and inhibition of collagen synthesis, the rise in collagenase synthesis and fall in collagenase inhibitor levels **(23)**.
Bleomycin is one of the treatment options for keloids and hypertrophic scars because it prevents the production of DNA, RNA, and proteins, which prevents collagen from being stimulated by the high amounts of TGFβ1 seen in scar tissue. **(24)**.
The goal of the present research was to examine the effectiveness and safety of using fractional co_2 in conjunction with bleomycin with triamcinolone acetonide for the management of hypertrophic scars and Keloids.
The current study included 40 patients with age ranged from 10-50 years old with hypertrophic scars and keloids; 23 males (57.5%) and 17 females (42.5%) and the majority of the patients in

this study were in the third decade of life. Another research found that although keloids might develop at any age, they were more prevalent in those between the ages of 10 and 30. **(25)**.

Fitzpatrick skin types III and IV were the most frequent in the patients, which is consistent with Prabhu et al revealed that keloids were more prevalent in dark-skinned populations and mostly occurred in people of African, Asian, and Hispanic heritage. **(26)**.

This research provides further proof that bleomycin is one of the many treatments available for hypertrophic scars and keloids, and it justifies a more prominent place among the many treatments available for these conditions. Additionally, it provides a number of treatment options that may be employed concurrently or in place of triamcinolone.

In this study, With no statistically substantial variation between the two groups, both medications improved the overall Vancouver scar scale score, vascularity score, and pigmentation score of hypertrophic scars and keloids. In addition, both drugs improved pliability of hypertrophic scars and keloids significantly but bleomycin showed better improvement and this came in agreement with ***Saray and Güleç*** who treated 14 patients with keloids and hypertrophic scars by Multiple jet injections of bleomycin was administered to each lesion every month and found improvement in all scar characteristics but pliability was better **(12)**.

Also, this came in line with ***Azzam et al*** who managed 30 patients with keloids and hypertrophic scars for a total of four sessions 6 weeks apart by fractional CO_2 laser only **(27)**.

Also, both medications considerably reduced the height of keloids and hypertrophic scars, although triamcinolone did so more effectively, which was consistent with ***Alexander et al*** who treated 25 patients with keloids and hypertrophic scars by fractional CO_2 laser followed by intralesional injection of triamcinolone and administered to each lesion every month and found improvement in all scar characteristics but height was better **(28)**.

In contrast ***Azzam et al*** detected that the scar height was the least factor to improve, especially in large keloids, and this could be postulated to the inability of the laser to reach the targeted depth **(27)**.

These outcomes were consistent with earlier studies by Haedersdal and Niwa et al., who discovered that shallow burn scars responded more favorably than deeper ones. Deeper dermal fibrotic components may be untreated because of the laser light's 400–1000 m dermal dermal penetration. The fact that this trial used a dual modality of triamcinolone and fractional co_2 laser, as opposed to previous published investigations that just used fractional co_2 laser, may account for the higher height increase. **(29, 30)**.

Additionally, parameters were modified in accordance with skin phototype, and SmartPulse was utilized to target the dermis without bulk heating and produce collagen remodeling. **(31)**.

For phototypes with darker complexion, more spacing was utilized. To allow for additional collagen remodeling to take place in the keloid bulks, a dwelling time of 600 μs was employed for hypertrophic scars and 1000 μs for keloids. For keloid instances, additional stacking was employed to get the desired depth. **(31)**.

In this study, pigmentation score improved in both groups with no statistically substantial variation and this came in agreement with ***Azzam et al*** who discovered that hypertrophic scars' pigmentation improved, indicating that those with low-height hypertrophic dyspigmented scars are the greatest responders. **(31)**.

There was no statistical substantial variation between the two groups in terms of clinical response. In group A, excellent improvement reported for 7 patients (35%), good improvement for 3 patients (15%), fair improvement for 8 patients (40%), poor improvement for 2 patients (10%). In group B, excellent improvement reported for 5 patients (25%), good improvement for 6 patients (30%), fair improvement for 6 patients (30%), poor improvement for 1 patient (5%), no improvement for 2 patients (10%).

No improvement for 2 patients in triamcinolone group may be explained by the long duration of lesions more than 10 years duration and these patients may be non-responder to steroid **(32)**.

Percentage of improvement in this study is lower than study of ***Khan et al*** who treated 82 patients with hypertrophic scars and keloids by intralesional bleomycin and 82 patients with

hypertrophic scars and keloids by intralesional triamcinolone acetonide every month for a duration of 6 months. In the bleomycin group, 82% of patients had a drop in their score of 75–100%, whereas in the triamcinolone group, 70% of patients saw a reduction in their score of 50–75%. The average length of the lesions in Khan's research was 4 months, the majority of the patients had less than two keloids, the total number of sessions was 6 more than in our study, and the follow-up period was 6 months long. These factors may account for the disparities between the two studies. **(33)**.

According to some writers, scars that are less than a year old react more favorably to laser modulation than older scars, which may be explained by the existence of cytokines and growth factors that are involved in the early stages of wound formation. **(30)**.

As regard patient's satisfaction, there was no statistically significant difference between both groups. In group A, 2 patients (10%) were not satisfied, 6 patients (30%) were slightly satisfied, 5 patients (25%) were satisfied, 7 patients (35%) were very satisfied. In group B, 1 patient (5%) were not satisfied, 5 patients (25%) were slightly satisfied, 6 patients (30%) were satisfied, 8 patients (40%) were very satisfied. These results correlated with ***Azzam et al*** who found Three of the 12 keloid patients who finished the trial were very happy with their treatment, whereas the other three patients were only somewhat satisfied. In the group of patients with hypertrophic scars, 2/7 (28.6%) patients rated the effectiveness of the treatment as outstanding, 1/7 (good), 2/7 (moderate), and 2/7 (poor). Due to high patient expectations and the fact that the considerable decline in the VSS after three months of treatment was mostly caused by better scar pliability rather than changes in scar vascularity and pigmentation, several patients were not or were only partially happy. These patients could need additional sessions and follow-up care for a longer time. **(27)**.

El-Zawahry et al. treated fifteen patients with hypertrophic and keloidal scars with three co_2 fractional laser sessions every 4-6 weeks and discovered that hypertrophic scars showed substantial textural advancement in all patients and a substantial reduce in Vsss when compared to keloids. The score improvement was considerably greater in hypertrophic scars when compared to keloids in both groups. **(34)**.

This was explained by the nature of each scar type, hypertrophic scars do not extend beyond the initial site of injury and tend to regress over time, keloids typically project beyond the original wound margins and almost never regress **(35)** and due to the increased proliferative activity of keloidal fibroblasts and lower rates of apoptosis and the amount of collagen produced by keloids is 20 times more than that of normal skin and 3 times higher than that of hypertrophic scars. **(36)**.

Only a few mild side effects were reported with each medicine in terms of side effects. Hyperpigmentation (15-75%) was the side effect of bleomycin used to treat keloid and hypertrophic scars that was most often observed. Fortunately, this side effect was lesser in this study (10%) than other reported studies treated by intralesional bleomycin only such as study of ***Payapvipapong et al*** **(37)**.

This difference may be explained by the role of laser in this study as similar as the study of ***Azzam et al*** who discovered that hypertrophic scars' pigmentation improved, indicating that those with low-height hypertrophic dyspigmented scars are the greatest responders. **(27)**.

In contrast, ***Bodokh*** discovered no hyperpigmentation in patients with lighter skin types but only little residual pigmentation in patients with Fitzpatrick skin Type III, and the variations between this research and the investigations of Bodokh and Espaa may be explained by the variations in the skin types of these studies. **(38)**.

The second most common side effect was pain at site of bleomycin injection and this side effect was absent in this study due to topical application of bleomycin within two minutes after laser session and due to effect of local anesthesia applied 60 minutes before session. In contrast, most studies reported pain at site of bleomycin injection **(39)**.

In patients treated with triamcinolone group, telangiectasias (10%) and hypopigmentation (10%) were observed in our study and this comes in agreement with ***Ahuja and Chatterjee*** and ***Viera et al*** **(40**, **41)**.

We used dermoscopy to examine the vascular patterns in keloids and hypertrophic scars before and after fractional co_2 laser treatment, followed

by topical applications of either bleomycin or triamcinolone acetonide. To our knowledge, this is the first study to do so, and we discovered that arborizing, linear, and comma-shaped vessels significantly improved in both groups without any correlation between dermoscopic changes and clinical changes as measured by the Vancouver scar scale score.

Dermoscopy before and after fractional co_2 laser treatment, followed by topical administration of either bleomycin or triamcinolone acetonide, was used to characterize the vascular patterns in keloids and hypertrophic scars.

The current study is constrained by the small patient population, hence further research is needed to support our findings.

CONCLUSION

With no statistically substantial variation between the two groups, both medications improved the overall Vancouver scar scale score, vascularity score, and pigmentation score of hypertrophic scars and keloids. Both medications considerably increased the pliability of keloids and hypertrophic scars, although bleomycin did so more effectively. Both medications considerably reduced the height of keloids and hypertrophic scars, although triamcinolone did so more effectively. Treatment of difficult hypertrophic scars and keloids was made possible by this combination of laser and laser-assisted administration of triamcinolone acetonide or bleomycin. When compared to keloids in both groups, the score improvement in hypertrophic scars was much greater. Hyperpigmentation was the main adverse effect of bleomycin but telangiectasia and hypopigmentation were the main adverse effects of triamcinolone acetonide.

STATISTICAL ANALYSIS

Data were gathered, edited, coded, and put into IBM SPSS version 23 of the Statistical Package for Social Science. When the quantitative data were parametric, they were shown as means, standard deviations, and ranges; when they were non-parametric, they were displayed as medians and interquartile ranges (IQR). Qualitative factors were also shown as percentages and numbers. The mean (average) is the middle value in a collection of discrete numbers; it is the sum of values divided by the total number of values. The measure of dispersion of a group of data is the standard deviation (SD). As opposed to a high SD, which shows that the values are dispersed across a greater range, a low SD implies that the values tend to be near to the established mean. The Chi-square test was used to compare groups using qualitative data. Utilizing an independent t-test, two groups with quantitative data and parametric dispersion were compared. The Mann-Whitney test was used to compare two groups utilizing quantitative data and a non-parametric distribution. The Kruskall Wallis test was utilized to compare more than two groups utilizing quantitative variables and a non-parametric distribution. Willcoxon test was used to compare two matched groups utilizing quantitative variables and a non-parametric distribution. The allowable margin of error was set at 5%, while the confidence interval was set at 95%. Consequently, the p-value was deemed significant as follows:

– $P > 0.05$: Non significant
– $P < 0.05$: Significant
– $P < 0.01$: Highly significant.

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