Comparison of the efficacy and safety of intralesional triamcinolone injection with the combination of triamcinolone, five fluorouracil, and hyluronidase enzyme in the treatment of keloids and hypertrophic scars

Ahmad E. Mohamed[a], Radwa E. Mahmoud[b]

[a]Plastic Surgery, Faculty of Medicine, Suez Canal University, Ismailia, Egypt, [b]Dermatology and Venereology, Faculty of Medicine, Suez Canal University

Correspondence to Ahmad E. Mohamed, MD, Department of Surgery, Faculty of Medicine, Suez Canal University, PO Box 112, Ismailia, 41511, Egypt. Tel: +01147776322; e-mail: rivercruise85@gmail.com

Received: 8 September 2023
Revised: 20 September 2023
Accepted: 2 October 2023
Published: 7 December 2023

The Egyptian Journal of Surgery 2023, 42:1007–1016

Hypertrophic and keloids scars are frequent benign disorders. These disorders occur due to the deposition of aberrant collagen in the scar tissue and can cause significant clinical presentations such as itching, discomfort, and disfigurement. Many therapeutic approaches have been proposed for their treatment without any acceptable outcomes.

Methods

After receiving ethical committee approval, a randomized prospective control trial was done in the clinic of plastic surgery at Suez Canal University Hospital for 3 months, from June 2023 to September 2023. 30 patients of both sexes and above the age of 14 were enrolled in the study and classified into two equal groups of 15 each: group (A) patients injected with triamcinolone alone, and group (B) patients injected with the combined therapy. All lesions were evaluated at 4, 8, and 12 weeks of injection. Scars were evaluated by the patient and observer scar assessment scale (POSAS) score. Complications such as atrophy of the skin, superficial ulcers, and telangiectasia have also been reported during or after injection.

Results

At 12 weeks of injection, both doctors and patients gave remarkably lower patient and observer scar assessment scale scores compared with those before injection, and there was a statistically significant difference between both groups. Group (B) scars improved more than group (A) scars in terms of itching, discomfort, pain, movement limitation, and aesthetic concern. Recurrence occurred only in group (A) patients.

Conclusion

The injection of the combined solution is effective more than triamcinolone alone. It results in a faster response, and an acceptable aesthetic outcome with few adverse effects.

Keywords:
hypertrophic, keloid, therapy

Egyptian J Surgery 42:1007–1016

1110-1121

Introduction

Hypertrophic and keloidal scars are frequent benign disorders [1–3]. These disorders cause significant clinical presentations such as disfigurement, itching, and discomfort [1,4,5]. With different success rates, a variety of treatments for keloid have been promoted, including intralesional injection of chemotherapeutic agents, laser phototherapy, radiation, cryotherapy, topical application of silicon sheets, and surgical excision [6,7].

The purpose of this study is to assess the safety and efficacy of a combined intralesional injection of five Fluorouracil (5-FU), TAC, and hyluronidase enzyme for the treatment of hypertrophic and keloidal scars.

Methods

After receiving ethical committee approval (the study had the approval of the local Institutional Review Board and the Research Ethics Committee, Faculty of Medicine, Suez Canal University on July 25, 2023, with the approval code 5409#), All participants provided written informed consent to participate in the study. An interventional clinical study was done in the clinic of plastic surgery at Suez Canal University Hospital for 3 months, from June 2023 to September 2023. Thirty patients of both sexes and above the age of 14 with keloids or hypertrophic scars ranging from 1 cm to 5 cm in size were included in the study.

The patients were assigned randomly into two groups using simple randomization. The person in charge of

 DOI: 10.4103/ejs.ejs_203_23

the allocation schedule was not present. For allocation, random numbers were employed through a computer-generated table [8] (ratio 1 : 1). Group (A) patients injected triamcinolone injection alone, and group (B) patients injected the combined therapy.

All patients who had scar treatment in the previous six months, a medical history of kidney disease, abnormal enzymes of the liver functions, or an abnormal white blood cell count were excluded from the trial. Also, after counselling and excluding pregnancy and breast feeding, females of childbearing age were chosen.

A detailed medical history was obtained, a clinical examination was carried out, and photographs and dimensions of all lesions were taken. All patients had a complete blood picture and liver and kidney functions before (baseline) and after the research.

Triamcinolone is used in its 40 mg/mL acetonide form, which is sold in 1 mL ampoules. 5 FU is commercially available in 10 mL ampoules containing 50 mg/mL. Ampoules containing 500 IU of hyaluronidase enzyme (testicular ovine freeze-dried powder) are available for purchase.

In each group, just deep into the scar, 1% xylocaine was injected through the margin of the scar rather than through the healthy skin. Once weekly, TAC intralesional injection at a dose of 10 mg was administered to participants in group (A) patients, while in group (B) patients, the combination therapy was received once a week through an intralesional injection of a reconstitution of hyaluronidase using 2.7 mL of 5 FU and 0.3 mL of triamcinolone. A 1 cc insulin syringe with a 27-gauge needle was used to inject the therapeutic solution. Five units of the solution were given, covering an area of 0.5×0.5 cm^2, so a scar of 1 cm^2 will require four injections. This dose was applied to both study groups in the same manner. The treatment was given by an investigator who was not aware of the injection. The greatest dose administered in a single session was 2 ml, in each group the solution was injected into the tissue mass of hypertrophic scars and keloids, as well as fibrotic regions (hardened tissue), until slight blanching was obtained. Each group received eight doses at weekly intervals. The lesions were evaluated by the second researcher at 4 and 8 weeks of treatment, as well as 4 weeks after treatment was completed.

The patient and observer scar assessment scale (POSAS) known to be a valid and reliable technique for measuring hypertrophic and keloid scars in a clinical situation, was used to assess the impact of therapeutic intervention. The POSAS is divided into two domains: an observer scale of six questions and a patient-reported scale of six questions. Each topic is graded on a Likert scale of one to ten, with 'one' representing 'normal skin' and 'ten' representing the 'worst scar imaginable' (Fig. 1). Each domain can be added together to obtain the individual patient scare assessment scale (PSAS) and observer scar assessment scale (OSAS), as well as the total score. As a result, the overall score will range from 6 to 60, with higher scores indicating poorer scar quality. The OSAS has six clinical items: pigmentation, vascularization, surface roughness, thickness, surface area, and pliability.

Patients are asked to rate the following six characteristics on the PSAS: colour, rigidity, thickness, irregularity, irritation, and pain are all factors to consider. Furthermore, both parties can provide an overall assessment of the scar in comparison to normal skin, although this is not factored into the total score. The addition of a patient-reported scale to the clinician-determined scale distinguishes the POSAS as the first PRO scar instrument published [9].

Induration, erythema, and pruritus were graded on a five-point scale (0=no erythema, induration, or pruritus; 1=mild; 2=moderate; 3=severe; 4=extremely severe). When the intervention reduced the initial scar height by more than 50%, it was deemed effective. Complications such as atrophy of the skin, superficial ulcers, and telangiectasia have also been reported during or after therapy.

Patients were observed for 4 months following the end of treatment for any recurrence, such as scar reappearance or an increase in its size, that occurred after treatment completion.

Statistical analysis

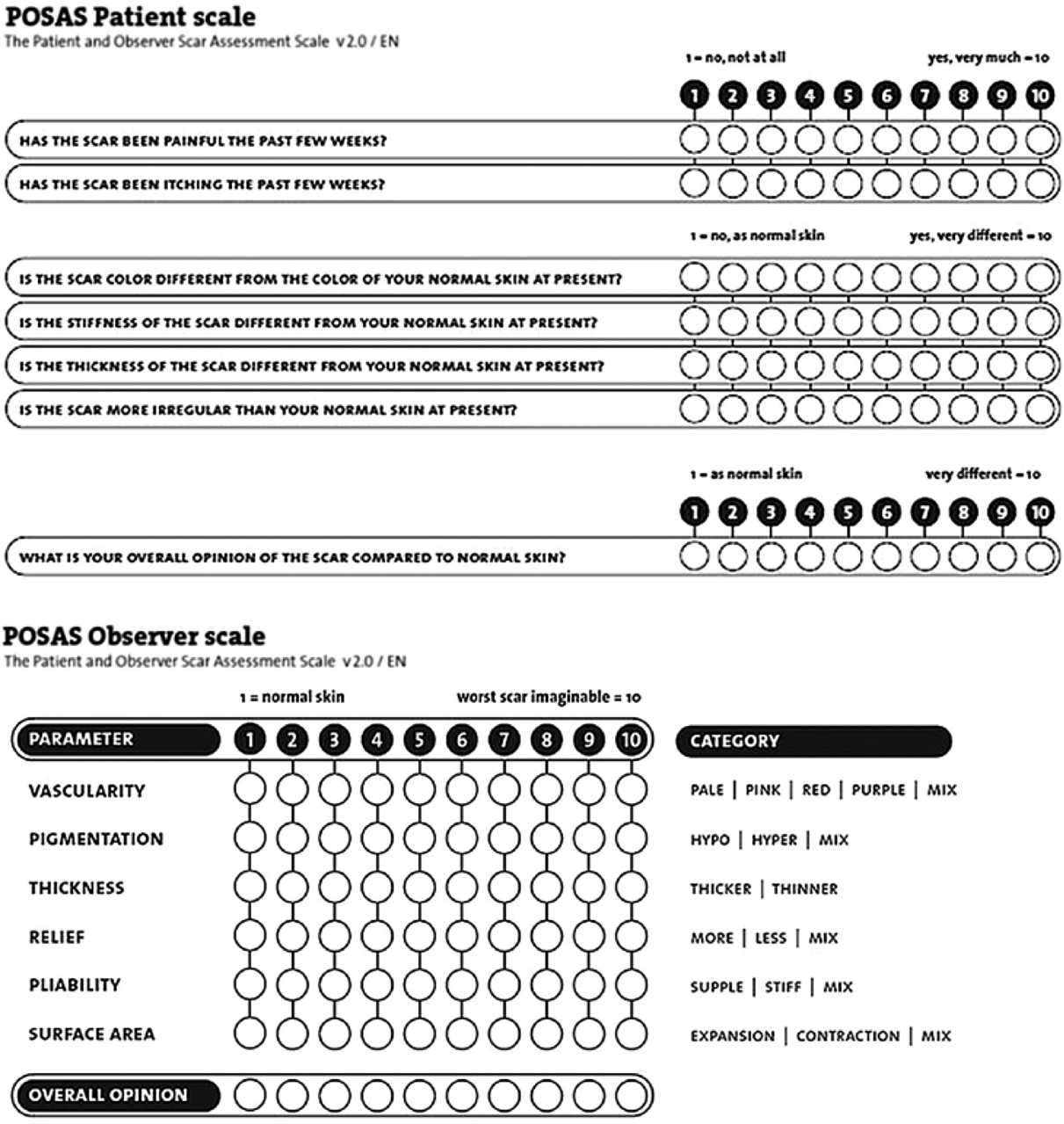
The IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp.) was used for data analysis. Categorical data were represented as numbers and percentages. A χ^2 test was used to investigate the relationship between the categorical variables. Alternatively, Fisher's Exact or Monte Carlo correction tests were used when more than 20% of the cells had an expected count less than 5. For continuous data, they were investigated for normality by the Shapiro-Wilk test. Quantitative data were expressed as range (minimum and maximum), mean, standard deviation, and median. A student *t*-test was used to compare two groups for

Table 1 Comparison between the two studied groups according to demographic data and clinical data

	Group A (n=15)	Group B (n=15)	Test of Sig.	P
Sex				
Male	9 (60%)	9 (60%)	χ^2=0.000	1.000
Female	6 (40%)	6 (40%)		
Age (y)				
Mean±SD.	24.8±4.8	27.3±7	t=1.120	0.272
Median (Min. – Max.)	25 (17–32)	28 (16–39)		
Duration of scar (years)				
Mean±SD.	9.9±3.1	10±3.2	t=0.058	0.954
Median (Min. – Max.)	9 (6.0–18)	9 (6–18)		
Type of scar				
Hypertrophic scar	7 (46.7%)	9 (60%)	χ^2=0.536	0.464
Keloid scar	8 (53.3%)	6 (40%)		

χ^2, Chi square test; FE, Fisher Exact; MC, Monte Carlo; SD, Standard deviation; t, Student t-test. [p:] represent the P value for comparing between the two studied groups. [*]: represent the Statistically significant which was at P less than or equal to 0.05. **Group A:** Received triamcinolone injection alone. **Group B:** Received the combined therapy.

Figure 1



Patient and observer scar assessment scale patient scale.

normally distributed quantitative variables. ANOVA with repeated measures for normally distributed quantitative variables to compare between more than two periods or stages. Post Hoc Test (adjusted Bonferroni) for pairwise comparisons, Friedman test for abnormally distributed quantitative variables to compare between more than two periods or stages, and Post Hoc Test (dunn's) for pairwise comparisons. The significance of the obtained results was judged at a level of 5%.

Results

Out of 30 patients included in this study, 18 (60%) were males and 12 (40%) were females. The gender distribution in both groups was nearly the same. The average age was 24.8±4.8 years for group (A) (range 17–32) and 27.3±7 years for group (B) (range 16–39). (*P*-value is 0.272.) This result is not statistically significant at *P*-value less than 0.05, so the requirement of homogeneity was met. (Table 1). The most common body sites were the upper limbs (45%), chest (20%), abdomen (20%), ear (10%), and lower limbs (5%).

Regarding scar duration, the average time in group (A) was 9.9±3.1 years, while 10±3.2 years in group (B). This result is not statistically significant at a *P*-value less than 0.05 (*P*-value = 0.954). (Table 1)

Regarding types of scars, in group (A) patients, hypertrophic scars were found in 46.7% of cases, while keloid scars were found in 53.3% of cases, while in group [(B)] patients, hypertrophic scars were found in 60% of cases, while keloid scars were found in 40% of cases. This result is not statistically significant at a *P*-value less than 0.05 (*P*-value = 0.464). (Table 1)

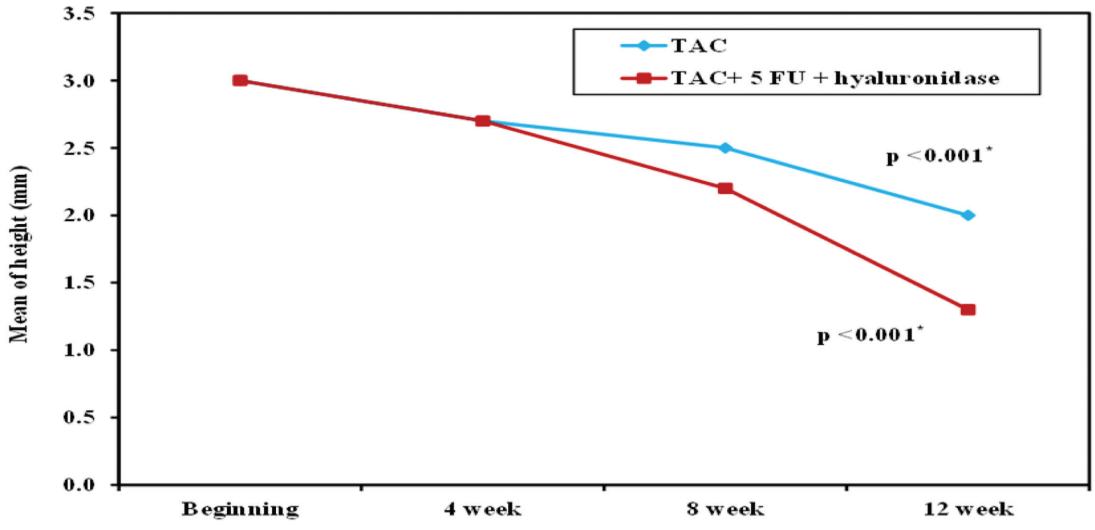
In both groups, the initial height of the scar was reduced at 4, 8, and 12 weeks of treatment (Fig. 2), but at 12 weeks of treatment, the reduction in scar height was greater in group (B) patients (combination therapy) than group (A) patients (monotherapy); this result was statistically significant at a *P*-value less than 0.05 (P-value = 0.004). (Tables 2).

The POSAS scores given by doctors and patients before treatments in each group were unremarkably similar, without any statistical difference between both groups (*P*-value = 0.069 in patient score and 0.765 in observer score). At 12 weeks of treatment, the scores given by both doctors and patients were significantly lower in comparison with before-treatment scores, and there was a marked and statistically significant difference between both groups (*P*-value <0.001 for both patient and observer). (Fig. 3 and Table 3).

At 4, 8, and 12 weeks of treatment, induration, erythema, and pruritus were reduced in both groups. (Table 4) There was a more favorable response in group (B) patients (combined therapy) in terms of reducing the induration, erythema, and pruritus scores (*P* values = 0.042, 0.031, and less than 0.001 at 4, 8, and 12 weeks, respectively). (Fig. 4 and Table 5)

Pain at the injection site was reported by 33.3% of those in group (A) patients and 13.3% of those in group(B) patients. Superficial ulceration developed in 26.7% of group (A) patients and 13.3% of group (B) patients;

Figure 2



Comparison between the different studied periods according to height.

Table 2 Comparison between the two studied groups according to height (mm)

Height	Group A (*n*=15)	Group B (*n*=15)	t	*P*
Beginning				
Mean±SD.	3.0±1.0	3±0.8	0.247	0.807
Median (Min. – Max.)	3 (1.9–5)	2.7 (2.1–4.2)		
4 weeks				
Mean±SD.	2.7±0.9	2.7±0.8	0.221	0.827
Median (Min. – Max.)	2.8 (1.8–4.5)	2.2 (1.9–3.9)		
8 weeks				
Mean±SD.	2.5±0.8	2.2±0.7	1.165	0.254
Median (Min. – Max.)	2.5 (1.6–4)	2 (1.3–3.2)		
12 weeks				
Mean±SD.	2±0.7	1.3±0.5	3.099*	0.004*
Median (Min. – Max.)	2 (1.1–3.5)	1 (0.6–2.1)		

SD, **Standard deviation**; **t**, **Student *t*-test**. p: represent the *P* value for comparing between the two studied groups. *: represent the Statistically significant which was at *P* less than or equal to 0.05. **Group A:** Received triamcinolone injection alone. **Group B:** Received the combined therapy.

Table 3 Comparison between the two studied groups according to patient and observer scar assessment scale score

	Group A (*n*=15)	Group B (*n*=15)	t	*P*
Observer				
Pretreatment				
Mean±SD.	26±3.8	26.3±1.9	0.302	0.765
Median (Min. – Max.)	26 (20–32)	27 (23–29)		
Posttreatment				
Mean±SD.	14.7±2.9	8.7±1	7.549*	<0.001*
Median (Min. – Max.)	14 (11–20)	8 (7–10)		
	***P*$_1$**	**<0.001***	**<0.001***	
Patient				
Pretreatment				
Mean±SD.	28.1±3.3	26.2±1.9	1.888	0.069
Median (Min. – Max.)	29 (22–33)	26 (23–29)		
Posttreatment				
Mean±SD.	17.1±2.7	9.1±1	10.864*	<0.001*
Median (Min. – Max.)	16 (13–22)	9 (8–11)		
	***P*$_1$**	**<0.001***	**<0.001***	

SD, **Standard deviation; t**, **Student *t*-test**. p: representing the p value for comparing between the follow up periods in each group. P_1: representing the *P* value for **Paired t-test for** comparing between pre and post in each group. *: representing the Statistically significant which was at *P* less than or equal to 0.05. **Group A:** Received triamcinolone injection alone. **Group B:** Received the combined therapy.

however, these ulcers resolved with conservative treatment without any substantial scaring. Atrophy of the skin and telangiectasia were seen in 33.3% of group (A) patients and 13.3% of group (B) patients. Hyperpigmentation appeared in 26.7% of group A patients and 20% of group B. There were no hematological adverse effects recorded in any of the individuals in the research. Recurrence occurred in 20% of group (A) patients and was not recorded in patients in group (B). (Table 6).

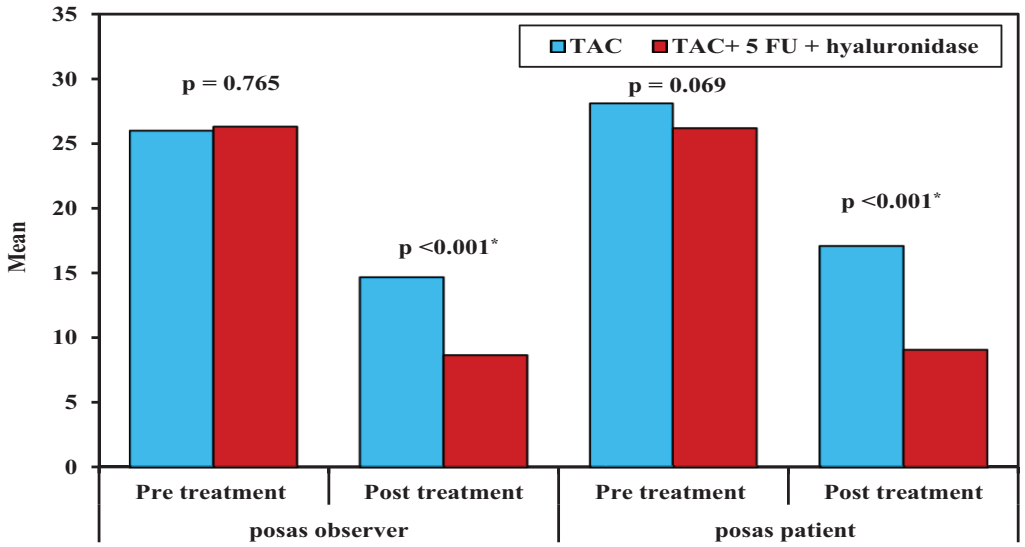
Discussion

Hypertrophic and keloids scars are frequent benign disorders [1,2]. They are caused by burns, trauma, surgery, and infections such as acne and folliculitis [3]. These disorders occur due to the deposition of aberrant collagen in the scar tissue and can cause significant clinical presentations such as itching, discomfort, and disfigurement [1,4]. Keloids expand beyond the borders of the wound, do not regress on their own, and are prone to recurrence despite medicinal or surgical treatment [5].

These lesions are more common in those with darker skin, their exact percentage varies from 4.5% to 16% [6,7]. however certain environmental and genetic variables may be involved, the precise etiology is yet unknown [3].

The specific pathophysiology of keloid formation is yet to be unknown, and there are numerous risk factors and theories [10,11]. keloid fibroblasts, in comparison with normal fibroblasts, create an inordinate amount of

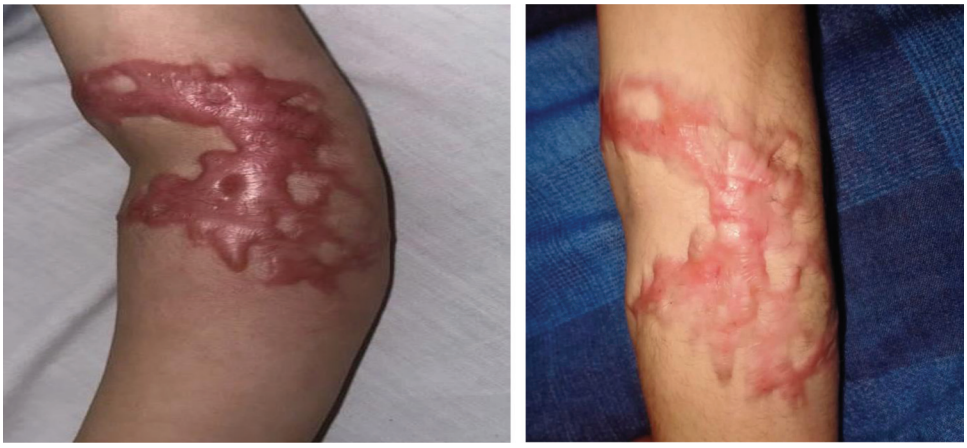
Figure 3



Group A: Received triamcinolone injection alone
Group B: Received the combined therapy

Comparison between the two studied groups according to patient and observer scar assessment scale score.

Figure 4



Picture of a post burn keloid scar at the outer side of the LT. elbow of 17 years old male patient demonstrating the effect of treatment after a combined therapy injection (lesion at presentation on the left side and response at 8 weeks of treatment on the right side).

collagen [11]. Keloids are primarily treated by decreasing the excessive proliferation of the fibroblastic activity of the scar tissue [12]. With different success rates, a variety of treatments for keloid have been promoted, including intralesional injection of chemotherapeutic agents, laser phototherapy, radiation, cryotherapy, topical application of silicon sheets, and surgical excision [10,12,13].

Triamcinolone has been frequently utilized in the management of hypertrophic and keloid scars. Steroids are anti-inflammatory, and they suppress collagen formation and interfere with protein synthesis and migration of the fibroblast while also increasing collagen breakdown. Triamcinolone is given in doses of 10–40 mg/ml every 4 to 6 weeks for a few months, or until the scar has been flattened [12,14]. Although recurrences occur in up to 50% of patients over time, there are certain undesirable adverse effects, such as atrophy of the skin, pigmentation, and telangiectasia [7,13].

With this unpredictability and major risks, researchers attempted to discover an ideal solution. Because these scars have been demonstrated to be hypermetabolic,

Table 4 Comparison between the different studied periods according to presence of erythema, induration and pruritus

	Pretreatment	4 weeks	8 weeks	12 weeks	Fr	*P*
Group A						
No	0	0	0	0		
Mild	0	0	3 (20%)	11 (73.3%)		
Moderate	3 (20.0%)	7 (46.7%)	9 (60%)	4 (26.7%)	39.808*	<0.001*
Severe	8 (53.3%)	5 (33.3%)	3 (20%)	0		
Extremely severe	4 (26.7%)	3 (20%)	0	0		
P_1		0.289	<**0.001***	<**0.001***		
Group B						
No	0	0	2 (13.3%)	10 (66.7%)		
Mild	0	5 (33.3%)	8 (53.3%)	5 (33.3%)		
Moderate	3 (20.0%)	6 (40%)	5 (33.3%)	0	42.321*	<0.001*
Severe	8 (53.3%)	4 (26.7%)	0	0		
Extremely severe	4 (26.7%)	0	0	0		
P_1		**0.013***	<**0.001***	<**0.001***		

Fr, **Friedman test**, Sig. bet. periods were done using **Post Hoc Test** (**Dunn's)**; SD, **Standard deviation**; **t**, **Student *t*-test**. p: representing the *P* value for comparing between the follow up periods in each group. P_1: representing the *P* value for comparing between Pretreatment and each other periods. *: representing the Statistically significant which was at *P* less than or equal to 0.05. **Group A:** Received triamcinolone injection alone. **Group B:** Received the combined therapy.

Table 5 Comparison between the two studied groups according to presence of erythema, induration and pruritus

EIP	Group A (*n*=15)	Group B (*n*=15)	χ^2	^{MC}P
Pre-treatment				
Mild	0	0		
Moderate	3 (20.0%)	3 (20.0%)	0.160	1.000
Severe	8 (53.3%)	8 (53.3%)		
Extremely severe	4 (26.7%)	4 (26.7%)		
4 weeks				
Mild	0	5 (33.3%)		
Moderate	7 (46.7%)	6 (40%)	7.728*	0.042*
Severe	5 (33.3%)	4 (26.7%)		
Extremely severe	3 (20%)	0		
8 weeks				
No	0	2 (13.3%)		
Mild	3 (20%)	8 (53.3%)		
Moderate	9 (60%)	5 (33.3%)	7.521*	0.031*
Severe	3 (20%)	0		
Extremely severe	0	0		
12 weeks				
No	0	10 (66.7%)		
Mild	11 (73.3%)	5 (33.3%)		
Moderate	4 (26.7%)	0	16.992*	<0.001*
Severe	0	0		
Extremely severe	0	0		

χ^2, **Chi square test**; MC, **Monte Carlo**. p: representing the *P* value for comparing between the two studied groups. *: representing the Statistically significant which was at *P* less than or equal to 0.05. **Group A:** Received triamcinolone injection alone. **Group B:** Received the combined therapy.

using an antimetabolite as a therapeutic option makes sense. Histological investigations show that fibroblasts are the cells that are overactive and responsible for the deposition of an excessive amount of collagen. These fibroblastic activities decrease in a dosage- and time-dependent manner [15].

Five Fluorouracil (5-FU) is an antimetabolite medication that acts through thymidylate synthase inhibition, RNA synthesis, and function interference. It inhibits Transforming growth factor (TGF)-b-induced production of the type I collagen gene in cellular human fibroblasts [14,16]. 5-FU is

Table 6 Comparison between the two studied groups according to complication

Complication	Group A (*n*=15)	Group B (*n*=15)	Test of Sig.	*P*
S Ulcer	4 (26.7%)	2 (13.3%)	χ^2=0.833	^{FE}P=0.651
Telangiectasia	5 (33.3%)	2 (13.3%)	χ^2=1.677	^{FE}P=0.390
Hyperpigmentation	4 (26.7%)	3 (20%)	χ^2=0.186	^{FE}P=1.000
Recurrence after 4 months	3 (20%)	0	χ^2=3.333	^{FE}P=0.224
Pain	5 (33.3%)	2 (13.3%)	χ^2=1.677	^{FE}P=0.390

χ^2, Chi square test; FE, Fisher Exact; MC, Monte Carlo; SD, Standard deviation. p: representing the *P* value for comparing between the two studied groups. *: representing the Statistically significant which was at *P* less than or equal to 0.05. **Group A:** Received triamcinolone injection alone. **Group B:** Received the combined therapy.

taken intralesional in modest dosages weekly or fortnightly and is considered a safe and successful option in keloid scar treatment [17,18]. When taken intralesional, there is no toxicity as long as the higher limit of the dose is not exceeded. Few of the adverse effects of 5-FU monotherapy, such as superficial ulceration and erythema, can be reduced by giving it combined with a lower and nontherapeutic dose of steroid (TAC) [19].

Hyaluronidase is an enzyme that hydrolyzes hyaluronic acid to increase connective tissue permeability. This temporarily reduces the viscosity of the intercellular cement, allowing the injected solution, exudates, and transudates to spread and improve absorption [20].

Blugerman and colleagues reported the management of scars, induration, retractions, and deformities over the nasal skin by a combination of 5-FU, hyaluronidase, and triamcinolone. the histopathological clarification of their effectiveness in the reduction of collagen fiber synthesis and rearrangement of their fibers, thus clarifying their positive therapeutic effect [20], but there was no clinical data about their effectiveness in the management of hypertrophic and keloidal scars.

Out of 30 patients included in this study, 60% were males and 40% were females. The sex distribution in both groups was almost the same. The average time of scar duration was 9.9±3.1 years in group A, while it was 10±3.2 years in group B.

In group (A) patients, hypertrophic scars were found in 46.7% of cases, while keloid scars were found in 53.3% of cases. In group (B) patients, hypertrophic scars were found in 60% of cases, while keloid scars were found in 40% of cases. The POSAS scores given by both doctors and patients before treatment in each group were unremarkably identical, without any statistically significant difference between both groups. After treatment, both doctors' and patients' scores were significantly lower than before treatment, with a clear and significant statistical difference between the two groups. The POSAS score regarding the efficacy of treatment in this study was better than the results recorded by Payapvipapong *et al.* [21], in their comparative study of intralesional Triamcinolone (TAC) and bleomycin for the management of hypertrophic and keloid scars; the same was true when compared with the results obtained by Darougheh *et al.* [1] and Khan *et al.* [13]. Zhuang Z *et al.* [22] found that 5-FU was recorded at a higher rate in patient self-assessments, while triamcinolone and 5-FU each had their own improvement regarding scar height and vascularity. Regarding the total POSAS score, there was no statistically significant difference between both drugs.

In this study, reductions in height, erythema, induration, and pruritus were more significant in group (B) patients (combination therapy) than group A (monotherapy). Darougheh *et al.* [1] and Khan *et al.* [13] observed nearly similar findings.

In this study, pain at the site of injection was felt in 13.3% of patients in group (B) and 33.3% of patients in group (A). Saha *et al.* [23] found that pain at the injection site was present in 95% of patients on 5-FU monotherapy. So, the addition of steroids may be the main factor in pain relief in this study. In 26.7% of patients in group (A) and 13.3% of patients in group (B), a superficial ulcer developed. Saha and Mukhopadhyay [23] found ulcers in 65% of cases with 5-FU monotherapy, demonstrating that the inclusion of a steroid decreases the rate of ulceration. All of these ulcers cured within two weeks at the end of treatment with conservative management, with no undesirable scarring. Some hyperpigmentation was noted in patients in both groups, which disappeared after 4 months of follow-up; the same was found by Sharma *et al.* [14].

Atrophy of the skin and some forms of telangiectasia were observed in 33.3% of patients in group (A) and 13.3% of patients in group (B), which was lower than

the 37% recorded in the study of Darougheh *et al.* [1]. Thus, monotherapy of either triamcinolone or 5-FU resulted in a greater degree of problems of some kind, which decreased when combined with triamcinolone, demonstrating the enhancement of these triple medications in keloid management and a reduction in side effects.

In this study, no patients experienced systemic or hematological adverse effects similar to those experienced by Nanda and Reddy [24].

In this study, 13.3% of cases showed recurrence 4 months after therapy completion only in group A that was absent in group B. Saha *et al.* [23] recorded a recurrence rate of approximately 36% of patients with monotherapy of triamcinolone and 5-FU, indicating that the combination therapy had greater therapeutic potential.

Conclusion

Combination therapy is a minimally invasive, cost-effective, and simple-to-implement treatment technique that produces consistent results while not invalidating or precluding other approaches in the event of failure. Also, it has a faster response, a more reliable outcome with fewer adverse effects, and a shorter period of treatment with more patient adherence to the management plan.

Financial issues: The cost of the intervention and the equipment will be paid by the researcher.

Acknowledgements

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

Availability of data and materials: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authorship: All authors had made substantial contributions to all of the following: (1) the conception and design of the study, (2) acquisition of data, data analysis and interpretation, (3) drafting the article and revising it critically, (4) final approval of the submitted version, (5) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved (6) each author believes that the manuscript represents honest work, if that information is not provided in another form.

Ethic's Approval and Patients' Consent: The study had the approval of the local Institutional Review Board and the Research Ethics Committee, Faculty of Medicine, Suez Canal University on July 25, 2023, with the approval code 5409#.

Financial support and sponsorship

Nil.

Conflicts of interest

The authors have no conflict of interest to declare.

References

1 Darougheh A, Asilian A, Shariati F. Intralesional triamcinolone alone or in combination with 5-fluorouracil for the treatment of keloid and hypertrophic scars. Clin Exp Dermatol 2009; 34:219–23.

2 Kelly AP. Medical and surgical therapies for keloids. Dermatology 2004; 17:212–8.

3 Robles DT, Berg D. Abnormal wound healing: keloids. Clin Dermatology 2007; 25:26–32.

4 Kakar AK, Shahzad M, Haroon TS. Keloids: clinical features and management. Part I. J Pak Assoc Dermatology 2006; 16:97–103.

5 Fitzpatrick RE. Treatment of inflamed hypertrophic scars using intralesional 5-FU. Dermatologic Surgery 1999; 25:224–32.

6 Davison SP, Dayan JH, Clemens MW, Sonni S, Wang A, Crane A. Efficacy of intralesional 5-fluorouracil and triamcinolone in the treatment of keloids. Aesthetic Surg J 2009; 29:40–6.

7 Muneuchi G, Suzuki S, Onodera M, Ito O, Hata Y, Igawa HH. Long term outcome of intralesional injection of triamcinolone acetonide for the treatment of keloid scars in Asian patients. Scand J Plastic Reconstructive Surg Hand Surg 2006; 40:111–6.

8 Graphpad Software to randomly assign subjects to treatment groups http://www.graphpad.com/quickcalcs/randomize1.cfm

9 Nicholas RS, Falvey H, Lemonas P, *et al.* Patient-related keloid scar assessment and outcome measures. Plastic Reconstructive Surg 2012; 129:648–56.

10 Jones CD, Guiot L, Samy M, Gorman M, Tehrani H. The use of chemotherapeutics for the treatment of keloid scars. Dermatology reports 2015; 7:5880.

11 Tuan TL, Nichter LS. The molecular basis of keloid and hypertrophic scar formation. Molecular Medicine Todaym 1998; 4:19–24.

12 Manuskiatti W, Fitzpatrick RE. Treatment response of keloid and hypertrophic sternotomy scars: comparison among intralesional corticosteroid, 5-fluorouracil, and 585-nm flashlamp-pumped pulsed-dye laser treatments. Archives of Dermatology 2002; 138:1149–55.

13 Khan MA, Bashir MM, Khan FA. Intralesional triamcinolone alone and in combination with 5-fluorouracil for the treatment of keloid and hypertrophic scars. Journal of Pakistan Medical Association 2014; 64:1003–7.

14 Sharma S, Bassi R, Gupta A. Treatment of small keloids with intralesional 5-fluorouracil alone vs. intralesional triamcinolone acetonide with 5-fluorouracil. Journal of Pakistan Association of Dermatologists 2012; 22:35–40.

15 Fujiwara M, Muragaki Y, Ooshima A. Keloid-derived fibroblasts show increased secretion of factors involved in collagen turnover and depend on matrix metalloproteinase for migration. Br J Dermatol 2005; 153:295–300.

16 Wendling J, Marchand A, Mauviel A, Verrecchia F. 5-Fluorouracil blocks transforming growth factor-β-induced α2 type I collagen gene (COL1A2) expression in human fibroblasts via c-Jun NH2-terminal kinase/activator protein-1 activation. Molecular Pharmacology 2003; 64:707–13.

17 Uppal RS, Khan U, Kakar S, Talas G, Chapman P, McGrouther AD. The effects of a single dose of 5-fluorouracil on keloid scars: a clinical trial of

timed wound irrigation after extra lesional excision. Plastic Reconstructive Surg 2001; 108:1218–24.

18 Ogawa R. The most current algorithms for the treatment and prevention of hypertrophic scars and keloids. Plastic and Reconstructive Surgery 2010; 125:557–68.

19 Gauglitz GG. Management of keloids and hypertrophic scars: current and emerging options. Clin Cosmetic Investigation Dermatology 2013; 6: 103–14.

20 Blugerman G, Schavelzon D, Wexler G. Five Fluorouracil, Hyaluronidase, and Triamcinolone in the Nasal Region [Internet]. Miniinvasive Techniques in Rhinoplasty. XX: In Tech; 2016. Available from: http://dx.doi.org/10.5772/62068

21 Payapvipapong K, Niumpradit N, Piriyanand C, Buranaphalin S Nakakes A. The treatment of keloids and hypertrophic scars with intralesional bleomycin in skin of color. J Cosmet Dermatol 2015; 14:83–90.

22 Zhuang Z, Li Y, Wei X. The safety and efficacy of intralesional triamcinolone acetonide for keloids and hypertrophic scars: A systematic review and meta-analysis. Burns 2021; 47:987–998.

23 Saha AK, Mukhopadhyay M. A comparative clinical study on role of 5-flurouracil versus triamcinolone in the treatment of keloids. Indian Journal of Surgery 2012; 74:326–9.

24 Nanda S, Reddy BSN. Intralesional 5-Fluorouracil as a Treatment Modality of Keloids. Dermatologic Surgery 2004; 30:54–7.