RESEARCH ARTICLE

Comparison of intralesional triamcinolone acetonide alone and with 5-fluorouracil for the treatment of keloids

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Abstract

Objective: To compare the efficacy of intralesional triamcinolone acetonide alone and in combination with 5 -fluorouracil in the management of keloids.

Method: The prospective cross-sectional study was conducted at the Dermatology outpatient department, Ojha campus, Dow University of Health Sciences, Karachi, from April to September 2023, and comprised patients with keloids who were divided into group A receiving intralesional triamcinolone acetonide 40mg/ml alone, and group B receiving a combination of triamcinolone acetonide 40mg/ml and 5-fluorouracil 50mg/ml. The medication was given monthly for 6 months, and efficacy was assessed using the Vancouver Scar Scale on each visit before the injection. Data was analysed with SPSS version 26.

Results: Of the 66 patients, 33(50%) were in group A; 19(57.6%) females and 14(42.4%) males with mean age 34.39±9.81 years. There were 33(50%) patients in group B; 20(60.6%) females and 13(39.4%) males with mean age 33.75±11.51 years. In group B, good to excellent response was seen in 31 (95%) cases compared to 23 (70%) in group A. Side effects such as atrophy (3 cases, 9.1%) and telangiectasia (2 cases, 6.1%) were more prevalent in Group A compared to atrophy (1 case, 3%) and telangiectasia (1 case, 3%) in Group B.

Conclusion: Intralesional triamcinolone acetonide in combination with 5-fluorouracil was found to be more effective with faster response and less side-effects compared to triamcinolone acetonide alone.

Keywords: Keloid, 5-fluorouracil, Triamcinolone acetonide, Vancouver scar scale. (JPMA 75: 1082; 2025)

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Introduction

Keloid is a Greek word meaning "Crab claw".[1-3] Keloid is a harmless, disfiguring, thick, raised, irregular but well-defined fibrous tissue that expands beyond the area of initial injury. It is not harmful to one's physical health, but may cause pain and itching, and sometimes get infected. Keloidal fibrous tissue consists of mainly type I and III collagen fibres. The definitive reason of keloid formation is not known but is more likely related to environmental and inherited factors.[4,5] Spontaneous regression is not a feature of keloid unless treated, otherwise it continues to grow over time.[6] Specific histological features commonly seen are over-production and accumulation of matrix proteins along with increased production and low apoptotic rate of fibroblasts in dermis.[7,8] Those commonly affected are aged 10-13 years. Upper body sites, like chest, shoulders, earlobes and upper back, are commonly involved compared to lower body areas.[9,10] The incidence of keloids ranges between 4.5% and 16% and types IV, V and VI are more common.[11] Besides, both genders are equally affected. Regarding trauma, about 5-15% of the wounds can heal with keloid formation. Keloids have high metabolic activity.[12] Keloids are commonly associated with itching and pain, but can also affect movement of skin if they are larger in size, or involve the joint area. There are many available treatment options apart from surgery, but triamcinolone acetonide (TAC), which is a long-acting glucocorticoid, is the most commonly given drug in injection form in the treatment of keloids because of its efficacy and easy availability. It is considered standard treatment in keloid management, alone or in combination.[13-15] Since keloids are notorious for high recurrence rate after treatment, especially after surgical excision, nonsurgical treatment modalities, like intralesional injection of effective medication are recommended for primary treatment nowadays.[16] Corticosteroids are effective in causing keloid regression by many different mechanisms, like, as an anti-inflammatory agent to decrease inflammation by inhibiting leukocyte and monocyte recruitment and subsequent phagocytosis.[17] They also cause hypoxia as they are potent vasoconstrictors, thus decreasing the oxygen and nutrients to the affected area.[18] They also have an anti-mitotic[19] effect by decreasing cell production of keratinocytes and fibroblasts, slowing re-epithelialisation and excess collagen formation. Furthermore, they decrease plasma protease inhibitors, thus allowing more collagen breakdown by

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collagenases. In some studies, clinically, the effect of corticosteroid injection alone was variable, with 50-100% regression in size and a recurrence rate of 33-50% after 1 and 5 years, respectively. Five-year recurrence rates after surgical excision followed by TAC administration were reported to be between 8% and 50% of cases. Difference in dosing, frequency and total treatment duration was observed among doctors in different settings.

Apart from its benefits, intralesional TCA injections may cause several unwanted side-effects, both local, such as telangiectasias, excessive hair growth, skin thinning and lipoatrophy, dyschromia (hypopigmentation and hyper-pigmentation), tissue necrosis and ulcerations and sometimes systemic effects, such as iatrogenic Cushing's syndrome. The chances of local side-effects are high when the surrounding normal skin is also injected with steroid while injecting into the keloid. Because of these side-effects, intralesional 5-fluorouracil (5FU) is being used in the management of keloid scars with good results.[20]

5-FU is a pyrimidine analogue with antimetabolite activity, and is commonly used as antineoplastic drug, but also inhibits collagen formation in vitro by decreasing fibroblast activity and blocking tumour growth factor-beta (TGF-β)-induced expression of the type I collagen gene in human fibroblasts. Due to this property, it is widely used worldwide in the management of hypertrophic and keloid scars with fewer side-effects.[21,22]

The current study was planned to compare the efficacy of intralesional TCA alone and in combination with 5-FU in the management of keloids.

Patients and Methods

The prospective, cross-sectional study was conducted at the Dermatology outpatient department (OPD), Ojha campus, Dow University of Health Sciences (DUHS), Karachi, from April to September 2023. After approval from the institutional ethics review committee, the sample size was calculated using OpenEpi[23] online software with two-independent sample *t*-test in line with literature[24] regarding Vancouver Scar Scale (VSS)[25] parameters, at 80% power and 0.05 significance level (alpha).

The sample was raised using non-probability consecutive sampling technique, and comprised patients of either gender aged at least 12 years with keloids. Those aged <12 years, and those with pregnancy or hypertrophic scar were excluded. The sample was divided on the basis random allocation table. Group A received intralesional TCA alone, while group B received a combination of TCA and 5-FU. In some cases, with history of anaemia, any recurrent infection, and any type of hypersensitivity reaction, blood tests, including complete blood count (CBC), haemoglobin (Hb) and total leukocyte count (TLC), were done before starting the treatment with 5-FU. In group A, TCA injection of 40mg/ml (0.3ml with 0.7ml xylocaine) was given using 27-gauge insulin syringe. In group B, 5-FU 50mg/ml (0.7ml) injection was given in addition to 40mg/ml TCA (0.3ml) in a concentration ratio of 7:3 using similar route and method. The injections, given 1cm apart, comprised 0.1ml of each of the solutions, and about 1.5-2ml of injection was given in one session. The injections were given monthly for 6 months. The effectiveness of the therapy was measured using the VSS (Table 1)[26] by two independent observers. The main parameter was the reduction in the height of keloid. Side-effects were also observed at each visit, like infection, ulceration, atrophy and telangiectasis. At the end of injection treatment, the patients were followed up for further 6 months.

Table-1: Vancouver Scar Scale (VSS) scoring pattern.

Vascularity		
	Normal	0
	pink	1
	red	2
	purple	3
Pigmentation		
	normal	0
	hypopigmentation	1
	hyperpigmentation	2
Pliability		
	normal	0
	supple	1
	yielding	2
	firm	3
	ropes	4
	contracture	5
Height (mm)		
	flat	0
	<2mm	1
	2-5mm	2
	>5mm	3
Total		13

Data was analysed using SPSS 26. Frequencies and percentages were computed for qualitative variables, while mean ± standard deviation were calculated for quantitative variable as the data was found to have a normal distribution. Independent sample t-test was used for intergroup comparisons, while paired sample t-test was used for pre-post comparison. Pearson's chi-square and Fisher's exact tests were used for the association of categorical variables. P≤0.05 was considered significant.

Results

Of the 66 patients, 33(50%) were in group A; 19(57.6%) females and 14(42.4%) males with mean age 34.39±9.81 years. There were 33(50%) patients in group B; 20(60.6%) females and 13(39.4%) males with mean age 33.75±11.51 years The commonest cause was surgery, followed by

Table-2: Basic characteristics of the patients.

Variables		Group A TCA n(%)	Group B TCA+5FU n(%)	*p*-value
Mean Age (years)		34.39±9.81	33.75±11.51	0.810
Gender				
	Male	14(42.4)	20(60.6)	0.139
	Female	19(57.6)	13(39.4)	
Sites	arms	7(21.2%)	8(24.2%)	
	Legs	1(3.0%)	2(6.1%)	0.653
	trunk	11(33.3%)	12(36.4%)	
	face	3(9.1%)	8(24.2%)	
	Others (Ear lobes)	4(12.1%)	10(30.3%)	
Aetiology				
	trauma	9(27.3)	3(9.1)	0.134
	surgery	18(54.5)	19(57.6)	
	spontaneous	4(12.1)	4(12.1)	
	None	2(6.1)	7(21.2)	

p-value calculated by using independent sample-test for continuous variables and Pearson's chi-square test for categorical variables; TCA: Triamcinolone acetonide, 5FU: 5-fluorouracil.

trauma, and the trunk was the most common site, followed by the arms (Table 2).

At the end of the treatment, group B patients showed more improvement across all VSS parameters compared to group A patients (Table 3).

Regarding treatment response, good to excellent response in group B was seen in 31 (95%) cases compared to 23 (70%) in group A. The response was poor to fair in 2 (5%) group B patients compared to 10 (30%) in group A. Reduction in pruritus was better in group B compared to group A, and there was no marked pain reduction in any of the groups (Table 4).

Regarding side effects, atrophy was seen in 3(%) group A patients and 1(%) group B patient, telangiectasia in 2(%) group A patients and 1(%) group B patient. No ulceration or systemic adverse effects were noted in any patient (Figure).

Regarding individual VSS parameters, there was significant improvement (reduction) in height (p<0.001), pliability (p<0.001), and vascularity (p<0.001) as compared to pigmentation (p=0.325). At 6-month post-injection follow-up, no recurrence or any serious side-effect was seen in any patient.

Table-3: Mean pre-injection and post-injection VSS scores.

	Groups	0 weeks	4 weeks	8 weeks	12 weeks	16 weeks	20 weeks	24 weeks
Pigmentation	TCA	1.21±0.99	1.21±0.99	1.21±0.99	1.21±0.99	1.21±0.99	1.21±0.99	1.18±0.983
	TCA+FU	0.33±0.73	0.33±0.73	0.33±0.73	0.33±0.73	0.33±0.73	0.33±0.73	0.33±0.73
Height								
	TCA	2.36±0.489	2.30±0.467	1.58±0.830	1.36±0.549	1.18±0.465	0.45±0.711	0.33±0.595
	TCA+FU	1.94±0.348	1.94±0.348	1.36±0.489	1.21±0.415	1.00±0.000	0.24±0.435	0.00±0.000
Pliability								
	TCA	3.00±0.000	3.00±0.000	3.00±0.000	2.00±0.000	2.00±0.000	2.00±0.000	1.36±0.489
	TCA+FU	3.18±0.528	3.18±0.528	3.06±0.242	2.58±0.614	2.52±0.508	2.00±0.000	1.52±0.508
Vascularity								
	TCA	1.06±1.059	1.09±1.100	1.09±1.100	1.09±1.100	0.88±0.893	0.88±0.893	0.70±0.918
	TCA+FU	1.61±0.609	1.61±0.609	1.61±0.609	1.61±0.609	1.21±0.485	1.12±0.415	1.12±0.415

VSS: Vancouver Scar Scale, TCA: Triamcinolone acetonide, 5FU: 5-fluorouracil.

Table-4: Intergroup comparison of baseline and post-intervention VSS scores.

Variables		Group A TCA Mean±SD	Group B TCA+5FU Mean±SD	*p*-value
Pigmentation	0 weeks	1.21±0.99	0.33±0.73	<0.001*
	24 weeks	1.18±0.98	0.33±0.73	<0.001*
	p-value	0.325	NA	
Height	0 weeks	2.36±0.48	1.94±0.34	<0.001*
	24 weeks	0.33±0.59	0.00±0.00	<0.001*
	p-value	<0.001*	<0.001*	
Pliability	0 weeks	3.00±0.00	3.18±0.52	<0.001*
	24 weeks	1.36±0.48	1.52±0.508	0.121
	p-value	<0.001*	<0.001*	
Vascularity	0 weeks	1.06±1.05	1.61±0.60	0.004*
	24 weeks	0.70±0.91	1.12±0.41	<0.001*
	p-value	<0.001*	<0.001*	

p-value was calculated by using paired sample t-test for within group comparison; and independent sample –t-test for between group comparison; VSS: Vancouver Scar Scale, TCA: Triamcinolone acetonide, 5FU: 5-fluorouracil, NA: Not applicable.

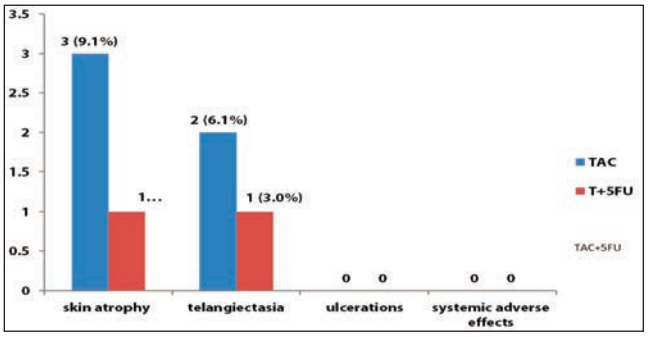

Figure: Intergroup comparison of side-effects.
TCA: Triamcinolone acetonide, 5FU: 5-fluorouracil.

Discussion

Keloid is a benign excessive growth of the fibrous tissue of skin that extends beyond the area of injury. The exact

reason of keloid occurrence is unknown, but is likely due to environmental and inherited factors. Keloid does not regress spontaneously without treatment, but often continue to grow with time.

In the current study, therapy assessment was done using VSS. The ratio of TCA and 5-FU in the current study was slightly higher and resulted in fewer side-effects compared to most other studies.[26,27] Similar to the current findings, studies done in 2012, 2018 and 2020 also showed more improvement among those treated with a combination of TCA and 5-FU[24,28].

Conclusion

There was a significant reduction in the size and height of scar among those treated with TCA in combination with 5-FU. The pace of improvement was fast, and there were fewer side-effects compared to those treated with TCA alone.

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Conflict of Interest: None.

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Author Contribution:
SB: Study design, data collection and final approval.
SAA: Data collection and critical revision.
MS & TI: Data collection and drafting.
FS: Drafting and data analysis.
HFW: Data analysis.