

Original Research Article

A comparative study on treatment of keloid with triamcinolone versus 5-fluorouracil and triamcinolone

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ABSTRACT

Background: The study was done to assess and compare the treatment of keloids with intralesional triamcinolone and combination of 5-fluorouracil and triamcinolone. Despite various options available, there is no universally accepted treatment for keloids. Our objective was to compare two regimens and establish superiority in terms of objective and subjective outcomes

Methods: A randomized parallel group study conducted in the Department of Plastic Surgery from January 2017 to June 2019. A total of 80 patients were taken with 40 each group.

Results: Though there was improvement in both regimens, this was more significant with combination regimen especially with vascularity, pliability, decrease in height and faster relief of symptoms like pain and itching.

Conclusions: Both were effective in treatment of keloids; triamcinolone alone was having relapse rate and combination therapy was more effective with faster results and few side effects.

Keywords: Keloid, Triamcinolone, 5-Fluorouracil

INTRODUCTION

Treatment of keloids is challenging for all clinicians, no standard treatment protocol exists. Though triamcinolone has been used as gold standard since 1980's, its efficacy is high in initial doses ranging from 50% to 90%, but recent data suggests nearly 10% to 50% of keloids tend to relapse with triamcinolone (TAC) after initial good response.

One among the new therapeutic options is antineoplastic agent 5-fluorouracil (5-FU), is a fluorinated pyrimidine antimetabolite that inhibits fibroblasts proliferation.^{1,2}

Studies comparing 5-FU with TAC have been limited, this randomized control study is aimed at comparing

results with TAC alone and combination of 5FU and TAC.^{3,4}

METHODS

This was a single blind randomized study conducted in Department of Plastic Surgery along with Department of Dermatology, SVIMS. The study protocol was approved by the institutional Ethics Review Committee. Informed consent was obtained from all the participants.

Patients were enrolled on outpatient basis between January 2017 to June 2019, well informed consent was taken from all the patients. A total of 80 patients were included with 40 patients each group on random basis.

Inclusion criteria of this study were all the patients aged 15 to 60 years with keloids were included, with history of more than 6 months, care was that no other therapies like scar massage, laser therapy, or pressure garments during the course of study. All keloids were well differentiated from hypertrophic scars.

Exclusion criteria of this study were any patients under the age of 15, pregnancy or lactation, with any renal failure or liver dysfunction, hematological disease or bone marrow suppression, any keloid with local infection (inflammation) or ulcer were not included in the study.

Detailed history and demographic parameters were recorded, including etiology and region of keloid. Etiology was divided into infective, traumatic, and, if there was no discernible etiology, spontaneous. Informed consent was obtained from all the patients.

Doses and interval

Insulin syringe of 27 gauge was used, in group of Triamcinolone alone TAC- 40 mg/1 ml, with maximum not exceeding 2 ml was given at every 4 weeks interval.

In the other group of triamcinolone with 5-FU, TAC dose was 40 mg/ml and 0.4-0.5 mg/ml of 5-FU was given every 4 weeks interval.

Intralesional injection

Injections were made with 27-gauge insulin syringe such that volume injected did not exceed 0.5 ml per square centimeter of keloid. Whenever necessary, multiple pricks were made 0.5 cm apart to ensure complete and uniform distribution

A maximum of 2 ml was injected per session. Injections were administered every 4 weeks till 16 weeks.

Keloid was defined as “resolved” when a total score of 2 or less was achieved on Vancouver scar scale (VSS).

All patients were evaluated before every injection and a final evaluation was performed 30 weeks after first dose. All evaluations were done by two independent observers who were blinded to the treatment groups. Evaluation was done objectively using VSS and subjectively by assessing pain and pruritus. Adverse effects at the time of injection and other complaints during the course of treatment were also recorded. VSS was originally designed by Sullivan et al to assess burn scars, which has since been extended to include other scars as well.^{5,6} For VSS, keloid height was measured with calipers; pliability was assessed by palpation; vascularity was assessed by visual inspection; and pigmentation was scored after blanching and comparing it with the surrounding skin. Blanching was achieved using a piece of clear plastic sheet. Pain and pruritus were scored on a three-point

scale as follows: 0=no pain or pruritus; 1=mild; 2=moderate; and 3=severe pain or pruritus.

Pain and pruritus scores were compared between the three groups using chi-square test for qualitative analysis and analysis of variance for difference in means of groups. Statistical analysis was carried out with SPSS software for Windows version 24.0 (Armonk, NY). A p value of <0.05 was considered to be significant.

RESULTS

Out of total 80 patients enrolled in the study; they were randomly distributed in two groups of 40 each. The youngest patient included in the study was 15 years old and the oldest was 60 years old. There were 24 males and 16 females in each group of the study. Spontaneous etiology (n=42) was the commonest etiology followed by traumatic (n=26) and infective (n=12). Pre-sternal region (n=44) was the most frequently involved region, followed by trunk (n=14) and extremities (n=14), and face (n=8). The baseline characteristics in terms of age, sex, etiology, and region involved were comparable in all three groups (Table 1). Mean pre-injection VSS scores for all treatment groups at every evaluation are presented in Table 2.

Table 1: Baseline characteristics of patients.

Variable	TAC	TCA and 5-FU	P value
Age (mean±SD) in years	28.35±6.11	29.9±10.19	0.41
Sex	N (%)	N (%)	
Male	24 (60)	24 (60)	0.72
Female	16 (40)	16 (40)	
Etiology			
Spontaneous	20 (50)	22 (65)	0.61
Traumatic	14 (35)	12 (20)	
Infective	6 (15)	6 (15)	
Region			
Presternal	22 (55)	22 (55)	0.66
Trunk	6 (15)	8 (20)	
Extremities	8 (20)	6 (15)	
Face	4 (10)	4 (10)	

All p values were greater than 0.05 (no statistically significant difference).

There was a reduction in height, vascularity, pliability, and pigmentation at every successive assessment in all two groups. There was good response with Triamcinolone initially and decreased or flattened response after 16 weeks, but response with combination therapy (TCA and 5-FU) was very much promising which continued till continued resolution of keloid even after 16 weeks. Statistically significant differences among groups in terms of reduction of vascularity and pliability were noted after the 4th week, while that of height and pigmentation were noted after the 12th week (Figure 1 to

3). Regarding pain and pruritis again though there was decrease in both groups but again symptomatic response for pain and pruritis was more pronounced in TCA and 5-FU group. Telangiectasias and skin atrophy were seen

most frequently in the TAC group (Table 3). Skin ulceration was a common problem in the 5-FU group (Figure 4).

Table 2: Mean pre-injection Vancouver scar scale scores.

VSS parameters	Group	0 week	4 weeks	8 weeks	12 weeks	16 weeks	24 weeks	36 weeks
Height	TAC	1.7±0.41	1.6±0.37	1.5±0.35	1.2±0.33	1.3±0.36	1.4±0.35	1.5±0.38
	TCA and 5-FU	1.8±0.31	1.5±0.32	1.1±0.27	0.6±0.24	0.5±0.25	0.6±0.23	0.6±0.23
Vascularity	TAC	1.85±0.37	1.45±0.32	1.05±0.27	0.75±0.27	0.55±0.17	0.55±0.19	0.65±0.23
	TCA and 5-FU	1.9±0.21	1.2±0.11	0.7±0.11	0.3±0.07	0.15±0.07	0.15±0.08	0.15±0.08
Pliability	TAC	2.8±0.42	2.2±0.32	2.0±0.31	1.8±0.22	0.6±0.23	0.8±0.22	0.9±0.24
	TCA and 5-FU	2.8±0.46	1.4±0.36	0.8±0.32	0.4±0.26	0.2±0.21	0.2±0.16	0.2±0.16
Pigmentation	TAC	1.85±0.37	1.5±0.32	1.45±0.27	1.35±0.22	1.15±0.23	0.85±0.24	0.85±0.24
	TCA and 5-FU	1.85±0.35	0.85±0.17	0.55±0.15	0.25±0.11	0.15±0.10	0.15±0.10	0.15±0.11
Pain	TAC	2.20±0.89	2.05±0.39	1.45±0.29	1.05±0.23	0.75±0.19	0.65±0.23	0.85±0.26
	TCA and 5-FU	2.15±0.86	1.15±0.26	0.55±0.11	0.15±0.06	0.05±0.05	0.02±0.02	0.02±0.02
Pruritis	TAC	2.85±0.44	2.45±0.34	2.05±0.24	1.45±0.21	0.75±0.24	0.85±0.26	0.85±0.24
	TCA and 5-FU	2.90±0.46	1.60±0.26	0.90±0.12	0.30±0.06	0.10±0.04	0±0	0±0

Values denoted as mean±SD.

Table 3: Summary of adverse effects.

Adverse effects	TAC	TCA and 5-FU
Skin atropy	2	0
Telangiectasia	5	0
Skin ulceration	0	3
Menstrual abnormalities	2	0
Systemic side effects	0	0

Values denote number of patients.

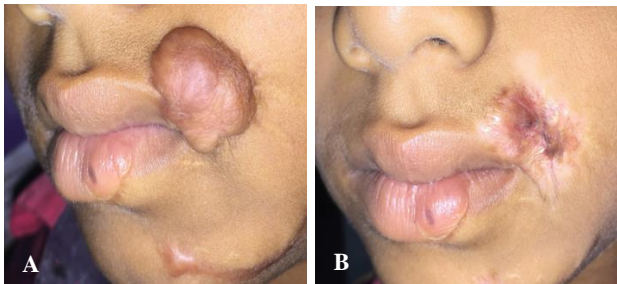


Figure 1 (A and B): Pre and post injection, TCA and 5-FU, decrease in size (height).

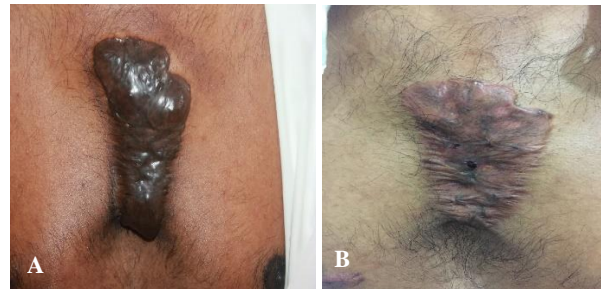


Figure 3 (A and B): Pre and post injection, TCA and 5-FU, decrease in size (height), pigmentation and vascularity.



Figure 2 (A and B): Pre and post injection, TCA and 5-FU, decrease in size (height).



Figure 4: Ulceration following injection of TCA and 5-FU.

DISCUSSION

Treating keloids is the most common challenge faced by all clinicians since many years. Still many clinicians consider treatment of keloids by 5-FU as experimental although many randomized controlled trials have proved the effectiveness of it.

Nanda et al and Kontochristopholus et al published a series of patients treated with 5-FU alone.⁷⁻⁹ Both of these studies reported favorable outcomes. Sadeghinia et al conducted a randomized controlled trial with 44 patients comparing efficiency of 5-FU and TAC, their study was similar to ours in terms of size, dose and concentrations.¹⁰ They reported 5-FU produced significantly better results compared to TAC. We too observed positive response in both groups and the improvement between base line and 6 months was statistically significant in both groups however, remission rate after TCA and 5-FU was lower than TAC alone.

In our study local side effects were more common with TAC group than in combination group (TCA and 5-FU), similar observations were found in Sadeghiania et al and Nanda et al group.^{7,10} But in our group local ulceration was more common in combination group (TCA and 5-FU). Similar side effect of local ulceration was reported to be more common in group using 5-FU by Kontochristopoulos et al and Srivastava et al.¹¹ But contrary to their study we had few side effect (ulceration) where the rate was less than 10% (n=3).

In our study both groups had pain during injection and post injection period, in combination regimen (TCA and 5-FU) post injection pain was more prolonged.^{12,13} Although not included in assessment, feedback from patients revealed that the injection, although painful, was tolerable, short lived, and relieved by oral analgesics alone.

A limitation of this study is the short duration of follow-up. All patients in our study were observed for 36 weeks, during which there was no recurrence. A long-term follow-up in such a prospective study is difficult. Our interaction with such patients leads us to believe that this is probably because the patient is unwilling to return when he is convinced that his "disease" has been apparently "cured." Perhaps a longer prospective study focusing on recurrence might prove more useful in this regard.

CONCLUSION

TAC, 5FU and their combination are all effective in keloid scars. A combination of TCA and 5-FU seems to offer the balanced benefit of faster and more efficacious response with lesser adverse effects when compared to TAC alone. Treatment has to be individualized and can be combined with one or more modalities to aim for better efficacy and safety.

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REFERENCES

1. Ghoshal K, Jacob ST. An alternative molecular mechanism of action of 5-fluorouracil, a potent anticancer drug. *Biochem Pharmacol.* 1997;53:1569-75.
2. Urioste SS, Arndt KA, Dover JS. Keloids and hypertrophic scars: review and treatment strategies. *Semin Cutan Med Surg.* 1999;18:159-71.
3. Bulstrode NW, Mudera V, McGrouther DA, Grobbelaar AO, Cambrey AD. 5-Fluorouracil selectively inhibits collagen synthesis. *Plast Reconstr Surg.* 2005;116:209-21.
4. Huang L, Cai YJ, Lung I, Leung BC, Burd A. A study of the combination of triamcinolone and 5-fluorouracil in modulating keloid fibroblasts in vitro. *J Plast Reconstr Aesthet Surg.* 2013;66:251-9.
5. Sullivan T, Smith J, Kermod J, McIver E, Courtemanche DJ. Rating the burn scar. *J Burn Care Rehabil.* 1990;11:256-60.
6. Truong PT, Abnoui F, Yong CM, Hayashi A, Runkel JA, Phillips T, et al. Standardized assessment of breast cancer surgical scars integrating the Vancouver Scar Scale, Short-Form McGill Pain Questionnaire, and patients' perspectives. *Plast Reconstr Surg.* 2005;116:1291-9.
7. Nanda S, Reddy BS. Intralesional 5-fluorouracil as a treatment modality of keloids. *Dermatological Surg.* 2004;30(1):54-6.
8. Kontochristopoulos G, Stefanaki C, Panagiotopoulos A, Stefanaki K, Argyrakos T, Petridis A, et al. Intralesional 5-fluorouracil in the treatment of keloids: an open clinical and histopathologic study. *J Am Acad Dermatol.* 2005;52(3):474-9.
9. Bijlard E, Steltenpool S, Niessen FB. Intralesional 5-fluorouracil in keloid treatment: a systematic review. *Acta Derm Venereol.* 2015;95:778-82.
10. Sadeghinia A, Sadeghinia S. Comparison of the efficiency of intralesional triamcinolone acetonide and 5-fluorouracil tattooing for the treatments of keloids. *Dermatol Surg.* 2012;38:104-6.
11. Srivastava S, Patil A, Prakash C, Kumari H. Comparison of intralesional triamcinolone acetonide, 5-fluorouracil, and their combination for the treatment of keloids. *Adv Wound Care.* 2017;6:11.
12. Sharma S, Bassi R, Gupta A. Treatment of small keloids with intralesional 5-fluorouracil alone vs. intralesional triamcinolone acetonide with 5-fluorouracil. *J Pakistan Assoc Dermatologists.* 2012;22:35-40.

13. Manuskatti W, Fitzpatrick RE. Treatment response of keloidal and hypertrophic sternotomy scars: comparison among intralesional corticosteroid, 5-fluorouracil, and 585-nm flash lamp pumped pulsed-dye laser treatments. *Arch Dermatol.* 2002;138:1149-55.

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