

Comparison of efficacy of intralesional 5-fluorouracil alone, intralesional triamcinolone acetonide alone and intralesional triamcinolone acetonide with 5-fluorouracil in management of keloids

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Abstract

Objective To evaluate the efficacy of intralesional 5-fluorouracil alone, intralesional triamcinolone acetonide alone and combination of intralesional triamcinolone acetonide and 5-fluorouracil in treatment of keloids.

Methods Ninety patients who fulfilled the inclusion and exclusion criteria were enrolled. Patients were randomly divided into three groups of 30 each. In group A; Intralesional 5-fluorouracil (5 FU) 50 mg/ml alone was used. In group B; Intralesional triamcinolone acetonide (TAC) 40mg/dl alone was used. In group c; combination of intralesional triamcinolone acetonide 40mg/dl (0.1ml) and 5-fluorouracil 50mg/ml (0.9ml) was used, on monthly basis for 6 months. Patients were assessed for efficacy, after 6 months of the treatment.

Results Efficacy was achieved in 70 cases in which 22 were from 5 FU group, 21 were from TAC group, and 27 were from 5 FU + TAC group. Statistically significant difference was found between TAC Vs 5 FU+TAC group i.e. p-value=0.02 and between 5 FU Vs 5 FU+TAC group i.e. p-value=0.04.

Conclusion The combination of 5-FU+TAC has better efficacy as compared to 5-FU alone group & TAC alone group in the management of keloids.

Key words

Intralesional 5-Fluorouracil, Keloids, Triamcinolone Acetonide.

Introduction

A keloid is a benign, well-demarcated area of fibrous tissue overgrowth that extends beyond the original defect.¹ Treatment of keloid is challenging for clinicians. It tends to recur after treatment, and does not regress spontaneously.^{2,3}

Keloids are most commonly seen in African-

American, Asian and Hispanic populations. Statistics on the incidence of keloids in specific populations vary greatly; however, an incidence of 4.5% to 16% has been reported in black and Hispanic patients. Keloids are least common in Caucasians and albinos.³

Various treatments like surgical excision, compression therapy, laser therapy, intralesional steroids, 5-fluorouracil (5-FU), radiotherapy, silicone gel and cryosurgery have been advocated but without convincing results and a cure is rarely achieved.^{4,5}

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Triamcinolone acetonide TAC injections are considered as the first treatment option for keloids. Triamcinolone acetonide acts by inhibiting protein synthesis and fibroblast migration. It also enhances degradation of collagen.⁶⁻⁹ Its efficacy has been demonstrated in earlier trials. However recent data suggests that 50% keloids do not respond to TAC injections. Furthermore, 9-50% of keloids that initially respond to TAC treatment ultimately relapse.

Some promise has been offered by 5-fluorouracil. It appears to shrink keloids safely while avoiding the tissue atrophy and telangiectasia as compared to steroid. The mode of action of this modality is by interfering with pyrimidine metabolism thus inhibiting fibroblast proliferation.^{6,7}

We conducted the study to find more efficacious treatment of keloids by comparing three treatment groups, none compared them directly in randomized controlled trial in our geographic region. It will help physicians to decide best treatment option for our patients hence improving their quality of life.

Methods

This randomized controlled trial was conducted in Department of Dermatology, Lahore General Hospital, Lahore. 90 patients with age > 18 years, of either sex, having size of keloids <5x5cm² were enrolled. Patients who had hypersensitivity to triamcinolone acetonide or 5-fluorouracil, pregnant or lactating females, patients with diabetes, hypertension, renal or liver insufficiency were excluded from the study. Diagnosis was made on clinical findings. Written informed consent was taken from the patients. A detailed history and examination was carried out. Patients were divided into three groups (A, B and C) each with 30 patients assigned by lottery method. In group A, patients

were given 50mg/ml 5-fluorouracil (5 FU) intralesional alone, while group B patients were given 40mg/ml triamcinolone acetonide (TAC) alone. In group C patients were given combination of 5 FU (0.1ml) + TAC (0.9ml). In each group injections were given on monthly basis for 6 months. Patients were seen on monthly basis. Efficacy was assessed after six months, which was defined as 51-100% improvement (flattening and decrease in size of lesion) after 6 months of treatment. Efficacy was graded as excellent (75-100%) good (50-75%) fair (25-50%) and poor (0-25%) and compared in three groups by using chi-square test taking p-value ≤0.05 as significant.

Results

In 90 patients with keloids, the mean age of patients in 5 FU group was 27.19±9.76 years, in TAC group was 29.10±9.47 years and mean age of patients in 5 FU+TAC group patients was 28.17±8.69 years.

There were 46 (51.11%) male patients and 44 (48.89%) females. The male to female ratio was 1.04:1.

Mean duration of keloids in 5 FU group was 5.03±3.01, in TAC group 6.30±3.01 years and in 5 FU+TAC group mean duration was 5.27±3.01 years.

Out of 90 keloids, 20 keloids were on earlobes, 18 on back, 22 were on shoulders and 30 were on front of chest.

Efficacy was achieved in total 70 cases in which 22 were from 5-FU group, 21 were from TAC group and 27 were from 5-FU + TAC group. Statistically significant difference in efficacy was found between the study groups TAC vs 5 FU+TAC i.e. p-value=0.02.

Table 1 Comparison of efficacy with study groups

		Study groups			Total
		5-FU	Steroid	5-FU+ Steroid	
Efficacy	Yes	22	21	27	70
	No	8	9	3	20
Total		30	30	30	90

Table 2 Comparison of efficacy with study groups

	5-FU vs steroid	Steroid vs combination	5-FU vs combination
Chi-square	0.0821	3.75	2.783
P-value	0.7745	0.0264	0.0477
Status	Insignificant	Significant	Significant

Table 3 Comparison of grading of effectiveness with study groups

		Study Groups			Total
		5-FU	Steroid	5-FU + Steroid	
Grading of effectiveness	Excellent	15	14	19	48
	Good	7	7	8	22
	Fair	7	6	3	16
	Poor	1	3	0	4
Total		30	30	30	90

Table 4 Comparison of grading of effectiveness with study groups

	5-FU vs. steroid	Steroid vs. combination	5-FU vs. combination
Chi-square	1.111	4.824	3.137
P-value	0.7743	0.1851	0.3709
Status	Insignificant	Insignificant	Insignificant

Likewise, statistically significant difference was found in efficacy between the study groups 5-FU vs 5 FU + TAC i.e. p-value=0.04. However, no significant difference in efficacy between the study groups 5-FU vs TAC. P-value=0.77 (Table 1 & 2).

Excellent response was found in 48 cases, good response was found in 22 cases, fair response was found in 16 cases while poor response was seen in 4 cases (Table 3 & 4).

Data was stratified for age, gender and duration of illness but no statistically significant

difference in efficacy was found in relation to these parameters.

Discussion

Keloid is an abnormal disfiguring scar that appears within 3-4 weeks of a provocative stimulus. Numerous studies have investigated various treatments for keloids, but the utility of these treatments and their efficacy when used in various combinations have not been clearly defined.

In this trial efficacy was achieved in 70 cases in which 22 were from 5 FU group, 21 were from TAC group, and 27 were from 5 FU + TAC group. Statistically significant difference was found between TAC Vs 5 FU+TAC group i.e. p-value=0.02 and between 5 FU Vs 5 FU+TAC group i.e. p-value=0.04.

A study by Muhammad Aslam khan *et al.*¹¹ also presented that the combination of triamcinolone acetonide and 5 fluorouracil (TAC+5 FU) is superior to triamcinolone acetonide alone therapy in the treatment of keloids and hypertrophic scars. 150 subjects in the study were divided into two equal groups of 75 (50%) each. Good to excellent results were seen in 51 (68%) cases in TAC group compared to 63 (84%) in combination group. Frequency of complications was 18(24%) and 6(8%) in TAC alone and combination group respectively. However there was no group comparing 5 FU efficacy alone in contrast to our clinical trial.

Davison *et al.*⁶ demonstrated results comparable to our study in a retrospective study of 102 keloids in which combination 5-FU/triamcinolone was superior to intralesional steroid therapy for treatment of keloids. The patients who received 5-FU/steroid combination had 92% average reduction in size of lesions compared to 73% in the group of patients who

received steroid alone. The results were found to be statistically significant ($p=0.05$) but similarly it compared two groups.

Study by Sagheer *et al.*¹² concluded that combination of 5 FU+Steroid had better efficacy in comparison with 5-FU alone. Efficacy was achieved in 32 cases in which 10 (33.3%) cases were from 5-FU group and 22 (73.3%) were from 5-FU+steroid group, which was statistically significant ($p=0.002$). This study was done in similar setting as ours but again lacked the comparison of third group.

Sharma *et al.*¹⁰ concluded that the combination of 5-FU and triamcinolone acetonide is a better modality of treatment of small keloids compared with 5-FU alone and these results are again comparable to our study. Good to excellent response was seen in 96% cases in combination group of steroid and 5-FU in contrast to 72% cases who received 5-FU intralesional alone.

The results of our study and also of the previous trials proved that combination group is more efficacious than 5 FU alone as well as TAC alone in the treatment of keloids.

Conclusion

Combination of intralesional 5 FU+TAC has better efficacy in the treatment of keloids in comparison with intralesional 5 FU alone and intralesional TAC alone. Now in future we should recommend the combination of intralesional 5-FU + TAC to effectively reduce the size of keloids.

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