

# Comparison of efficacy of intralesional 5-fluorouracil alone versus intralesional triamcinolone acetonide with 5-fluorouracil in small keloids

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## Abstract

**Objective** To evaluate the efficacy of intralesional 5-fluorouracil alone in comparison with the combination of intralesional triamcinolone acetonide and 5-fluorouracil in treatment of small keloids.

**Methods** Sixty patients who fulfilled the inclusion and exclusion criteria were recruited. Patients were randomly divided into two groups. In group A, intralesional 5-fluorouracil 50 mg/ml was used. In group B, combination of 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 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 ( $p=0.002$ ).

**Conclusion** In the treatment of small keloids the combination of 5-FU + steroid has better efficacy in comparison with 5-FU alone.

## Key words

Intralesional 5-fluorouracil, small keloids, triamcinolone acetonide.

## Introduction

A keloid is a benign, well-demarcated area of fibrous tissue overgrowth that extends beyond the original defect.<sup>1</sup> It is hyperproliferative growth, composed mainly of either type III (early) or type I (late) collagen. It tends to recur after excision, and does not regress spontaneously.<sup>2</sup> The cause is unknown, although both local and constitutional factors are involved. Burns or scalds and infected lesions, foreign material, either exogenous (e.g. suture

material) or endogenous (e.g. embedded hair), scarring acne, insect bite are risk factors which can lead to formation of keloids. Keloids develop most often on the chest, back, shoulders, and earlobes. They rarely develop on the face (with the exception of the jawline).<sup>3</sup> Keloids become raised and thickened within 3-4 weeks of the provocative stimulus. The lesion becomes a firm, pink or red plaque, which may grow for months or years. Lesions often assume a 'dumb-bell' configuration, but sometimes become bizarre and irregular. Keloids may lead to significant morbidity, as well as, pain, pruritus, restriction of movement and cosmetic disfigurement.<sup>4</sup>

Various treatments like surgical excision,

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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.<sup>5</sup> Due to its ability to recur in spite of adequate treatment and variable response to different therapies available, keloid poses a challenge to the physician. 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 and converting to 5-fluoro-2-deoxyuridine-5-phosphate (F-dump), which is potent inhibitor of thymidylate synthetase, thus DNA synthesis is blocked.<sup>6,7</sup>

Both softening and flattening of keloids have been attained by intralesional corticosteroid therapy. Triamcinolone acetonide acts by inhibiting protein synthesis and fibroblast migration. It also enhances degradation of collagen.<sup>8</sup>

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.<sup>9,10</sup>

Rationale of this study was to find the more effective treatment of keloids, which will help our patients in their treatment and improve their quality of life.

## Methods

This randomized controlled trial was conducted in Department of Dermatology, Lahore General

Hospital, Lahore. Sixty patients were included in the study with keloids of size  $<5 \times 5 \text{cm}^2$ . 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 patient. A detailed history and examination was carried out. Patients were divided into two groups (A and B) each having 30 patients by lottery method. In group A, patients were given 50mg/ml 5-fluorouracil intralesionally, while group B, patients were given a combination of 50mg/ml 5-fluorouracil (0.9ml) and 40mg/ml triamcinolone acetonide (0.1ml) intralesionally. In each group injections were given on monthly basis for 6 months. Patients were assessed on monthly basis for efficacy, which was defined as 51-100% improvement (flattening and decrease in size of lesion) after 6 months of treatment. Efficacy was compared in both groups by using chi-square test taking p-value  $\leq 0.05$  as significant.

## Results

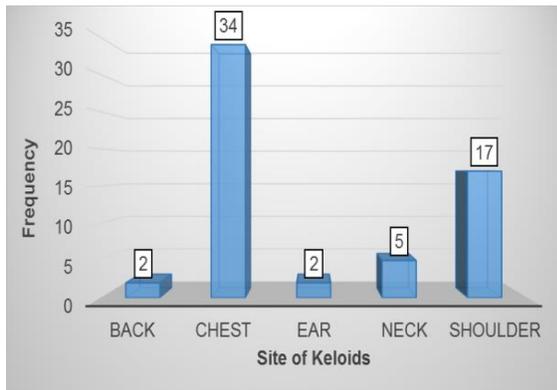
In this study we included 60 patients with small keloids. Mean age of the patients was  $23.38 \pm 35$  years. The minimum age of the patients was 13 years while the maximum age was 42 years. There were 17 (28.3%) male patients and 43 (71.7%) were females (**Table 1**). The male to female ratio was 1:2.5.

The mean duration of formation of small keloids was reported as  $5.26 \pm 4.85$  months. The minimum duration was 1 month while maximum duration was 24 months (**Table 1**).

**Table 1** Pre-treatment clinical characteristics of study population (n=60).

Age (years)	
Mean	23.38 $\pm$ 7.35
Minimum	13

Maximum	42
<i>Duration (months)</i>	
Mean	5.26±4.85
Minimum	1
Maximum	24
<i>Length (cm)</i>	
Mean	2.66±1.25
Minimum	1.0
Maximum	5.0
<i>Height (mm)</i>	
Mean	2.10±0.87
Minimum	1.0
Maximum	5.0



**Figure 1** Frequency distribution of site of keloids.

The mean length of keloids was 2.65±1.25cm with minimum and maximum values of 1 and 5 cm, respectively. The mean height of keloids was 2.10±0.87mm with minimum and maximum values of 1 and 5 mm, respectively (**Table 1**).

Frequency distribution of sites of keloids is shown in **Figure 1**. Chest was the most commonly affected site seen in 34 (56.7%) patients, followed by shoulders in 17 (28.3%), neck in 5 (8.3%) and ear and back in 2 (3.3%) patients each.

Efficacy (flattening or decreased size of lesion) 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. Similarly efficacy was not achieved in 28 cases in which 20 (66.7%) were from 5 FU group and 8 (26.7%) were from 5-FU + steroid group. Statistically significant difference was found

between the efficacy in study groups of the patients. The study results showed that the recurrence occurred in 3 cases and all of them were from 5-FU group.

## Discussion

Keloid is an abnormal disfiguring scar with claw like extensions in the normal skin. It becomes raised and thickened within 3-4 weeks of the provocative stimulus. Numerous studies have investigated effective treatments for keloids, but the utility of these treatments and their efficacy when used in various combinations have not been clearly defined.

In our trial, the mean age of the patients was 23.38±7.35 years. There were 17 (28.3%) male patients and 43 (71.7%) were females. There was more female presentation as compared to male patients. In more than 50% cases, keloids were found in chest region. The mean height of keloid was 2.10±0.87mm and the mean length was 2.65±1.25cm.

The study results showed that the 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. Similarly, efficacy was not achieved in 28 cases in which 20 (66.7%) were from 5 FU group and 8 (26.7%) were from 5-FU+Steroid group. Statistically significant difference in efficacy was found between the two study groups ( $p = 0.002$ ). The combination group showed significantly more efficacy in treatment of small keloids.

Sharma *et al.*<sup>11</sup> concluded that the combination of 5-FU and triamcinolone acetonide is a better modality of treatment of small keloids compared with 5-FU alone. Good to excellent response was seen in 96% cases in group of combination of 40 mg/ml triamcinolone acetonide (0.1 ml) and 5-FU 50mg/ml (0.9 ml) (B) in contrast to

72% cases only in group 50 mg/ml 5-FU intralesionally (A). The group B lesions showed better improvement than group A lesions in pruritus, pain, tenderness, restriction of movements and cosmetic problem. No recurrence was seen in any of the lesions.

Darougheh *et al.*<sup>5</sup> concluded that TAC + 5-FU combination was more acceptable to patients and produced better results than TAC alone. Both groups showed an acceptable improvement in nearly all parameters, but these were more significant in the TAC + 5-FU group. Good to excellent improvement were reported in only 20% of the patients in group 1 (TAC) and 55% of the patients in group 2 (TAC + 5-FU), which was statistically significant ( $P = 0.02$ ).

Davison *et al.*<sup>6</sup> demonstrated that the combination 5-FU/triamcinolone is superior to intralesional steroid therapy in the treatment of keloids. The patients who receive 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 ( $p = 0.05$ ).

Khan *et al.*<sup>12</sup> described in their study that good to excellent results were seen in 51 (68%) cases in group A (triamcinolone acetonide alone) compared to 63 (84%) in group B (triamcinolone acetonide + 5-fluorouracil). There was statistically strong evidence that the final scar height was better in TAC+5FU group ( $p < 0.001$ ). So it was concluded that the combination of triamcinolone acetonide and 5-fluorouracil is superior to triamcinolone acetonide therapy in the treatment of keloids and hypertrophic scars in terms of reduction in initial height of the scar.

Wu *et al.*<sup>7</sup> showed that surgical removal of auricular keloid followed by intralesional injection of low-dose 5-FU and steroid was an

effective method to treat auricular keloid and prevent its relapse. Normal auricular shapes were achieved in 77 (92.7%) cases and total effective rate was 100%.

## Conclusion

In the treatment of small keloids, combination of 5-FU + steroid has better efficacy in comparison with 5-FU alone with less recurrence rate.

## References

1. Köse O, Waseem A. Keloids and hypertrophic scars; are they two different sides of the same coin? *Dermatol Surg.* 2008;**34**:336-46.
2. Bollero D, Malvasio V, Catalano F, Stella M. Negative pressure surgical management after pathological scar surgical excision: a first report. *Int Wound J.* 2015;**12**:17-21.
3. Kischer C, Brody G. Structure of the collagen nodule from hypertrophic scars and keloids. *Scan Electr Microscop.* 1980 (Pt 3):371-6
4. Prabhu A, Sreekar H, Powar R, Uppin V. A randomized controlled trial comparing the efficacy of intralesional 5-fluorouracil versus triamcinolone acetonide in the treatment of keloids. *J Sci Soc.* 2012;**39**(1):19.
5. Darougheh A, Asilian A, Shariati F. Intralesional triamcinolone alone or in combination with 5-fluorouracil for the treatment of keloid and hypertrophic scars. *Clin Experiment Dermatol.* 2009;**34**:219-23.
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. *Aesthet Surg J.* 2009;**29**:40-6.
7. Gao R, Cao B, Hu Y, Feng Z, Wang D, Hu W *et al.* Human infection with a novel avian-origin influenza A (H7N9) virus. *New Engl J Med.* 2013;**368**:1888-97.
8. Wu X, Gao Z, Song N, Liu W. Clinical study of auricular keloid treatment with both surgical excision and intralesional injection of low-dose 5-fluorouracil and corticosteroids. *Zhonghua Yi Xue Za Zhi.* 2009;**89**:1102-5.

9. Alhady SM, Sivanantharajah K. Keloids in various races. A review of 175 cases. *Plast Reconstr Surg*. 1969;**44**:564-6.
10. Gupta S, Kalra A. Efficacy and safety of intralesional 5-fluorouracil in the treatment of keloids. *Dermatology*. 2002;**204**:130-2.
11. Sharma S, Bassi R, Gupta A. Treatment of small keloids with intralesional 5-fluorouracil alone vs. intralesional triamcinolone acetonide with 5-fluorouracil. *J Pak Assoc Dermatol*. 2012;**22**:35-40.
12. Khan MA, Bashir MM, Khan FA. Intralesional triamcinolone alone and in combination with 5-fluorouracil for the treatment of keloid and hypertrophic scars. *J Pak Med Assoc*. 2014;**64**:1003-7.