

# INTRALESIONAL INJECTION OF 5-FLUOROURACIL IN COMBINATION WITH TRIAMCINOLONE ACETONIDE IN KELOID TREATMENT

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## ABSTRACT

**Objective:** to evaluate the efficacy of 5-Fluorouracil (5-FU) and Triamcinolone Acetonide (TAC) injection combination in the management of Keloids.

**Methods:** Thirty patients with the diagnosis of keloid were treated with a combination injection of 5-FU & TAC. Objective assessments were done. Scar scales were assessed at baseline, 1 month, & 1 year follow-up.

**Results:** Ultrasound measurements shows a significant decrease in volume (baseline mean score:  $1,105 \pm 911.5$  mm<sup>3</sup>, 1-month follow up mean score:  $416.1 \pm 218.1$  mm<sup>3</sup>, 1-year follow-up mean score:  $431.2 \pm 253.6$  cu.mm,  $P = < 0.0001$ , respectively) and penetration depth of keloids (relative reduction between baseline and 12-month FU of 74.4%,  $P = < 0.0001$ ). The patient & observer scar assessment scales (POSAS) also show objective & subjective improvement in keloid size.

**Conclusion:** 5-FU in combination with TAC intralesional injection is effective for keloid management.

**Key words:** 5-Fluorouracil, Ultrasound, TAC

## INTRODUCTION:

Though the diagnosis is easy, the treatment of keloid is still the challenging one for the surgeons. Though various treatment options like surgical excision, cryotherapy, laser therapy, low-dose radiation, silicone sheeting, topical retinoids and intralesional injections of steroid, 5-fluorouracil (5FU) and bleomycin are available none of them consistently prevent recurrence. Of these, Triamcinolone acetonide (TAC), a long-acting glucocorticoid one of the popular drugs and has gained popularity and used either alone or in combination (clinical efficacy 50-100% and a recurrence rate of 9% - 50%). In 1999, Fitzpatrick first introduced 5-fluorouracil (5FU), a pyrimidine analogue for the treatment of keloid. 5FU is comparatively faster in scar flattening. Combining TAC with 5FU has a rapid scar-flattening response with fewer side effects. In this randomized study, the objective of comparing these three regimens viz. triamcinolone alone, 5-fluorouracil alone and a combination of triamcinolone and 5-fluorouracil in terms of subjective and objective outcomes, and adverse effects.

## MATERIALS AND METHODS

Patients and study methodology

### Inclusion criteria

- > 18 years of age
- < 65 years of age
- Keloid more than 2 years

### Exclusion criteria

- Immunosuppressive patient (either due to drugs or because of disease)
- Uncontrolled DM
- Patient on other modes of keloid treatment
- Infected/ ulcerated keloid
- Pregnancy

### Methodology

30 patients (18 females and 12 males) were enrolled in the clinical study after getting written informed consent. The mean age of the study group was 30.5. Keloids are mostly present on patients' chest, ear lobes, shoulders, and backs. keloids predominantly developed because of acne, trauma, surgery and spontaneously. Prior to each treatment, as well as at 1- and 12-month Follow-up, data were collected using digital photography, ultrasound, and standardized questionnaires (POSAS). All the patients received four intralesional injections of a combination of 5-FU (50 mg/mL) and a crystalline TAC suspension (10 mg/mL) at a ratio of 3: 1, till the blanching occurred. Injections were given at 21 days interval. The average injected volume per keloid: visit 1:

1 mL, visit 2: 0.8 mL, visit 3: 0.6mL and visit 4: 0.4mL. Ultrasound high-resolution B-mode-image sonogram was used for non-invasive analysis of the cutaneous depth and height of keloids. To assess both patients' and observers' opinions regarding the severity of scarring, we evaluated the keloids throughout the study by using the well-established POSAS.

## RESULT

### Ultrasound

Ultrasound examinations of 30 keloids showed decreases in skin extension and depth throughout the period. Altogether a reduction in skin extension by 65.2% was identified from the baseline and the 1- year follow up period. Skin penetration depth also showed noticeable improvement, reduced by 74.4% between baseline and 1- year follow up period.

### Patient and Observer Scar Assessment Scales (POSAS)

All the parameters in the patient score showed significant positive outcomes after this treatment. Pruritus and pain were drastically reduced by 57% and 55%, respectively. Scar thickness and stiffness also showed significant improvements, reduction of 43% and 42% lower at 1-year follow up period which is compared to baseline ( $P<0.0001$  for all measurements). The patients' overall feedback of the scars reduced by 39% till the end of the study ( $P<0.0001$ )

The observer data showed statistically significant improvements in all examined scar parameters. Scar pliability improved by 54% all over the study. Other scar features such as pigmentation, relief and thickness presented with scores by 46%, 45% and 44% reduction, respectively, ( $P<0.0001$  for all measurements). The observer's overall feedback of the examined scars showed improved by 52% from the baseline measurements and 1- year follow up period ( $P<0.0001$ ).



## DISCUSSION

Management of excessive scarring, especially keloids, remains challenging. Even though a group of patients benefited from conventional therapeutic methods such as surgical excision, cryotherapy, laser therapy, low-dose radiation, silicone sheeting, topical retinoids and intralesional injections of steroid, 5-fluorouracil (5FU) and bleomycin. Still there are reasonable number of keloids that seems not responding to these methods or it will recur after initial response to the treatments. 5-FU has been used for the management of keloids for many years. TAC acts by suppressing the cell proliferation, 5-FU by promoting apoptosis, thus leading to better results. Intralesional injections of 5-FU for the management of keloids had been studied well and have

showed good efficacy in randomized control trials, prospective clinical trials, and case series. 5-FU alone has been shown to give good results in treating keloids.

LaRanger and colleagues studied the efficacy of 5-FU as an adjunct after the removal of severe keloids. Weekly to bi-weekly injections given for a sum of four times starting 2 weeks after keloid removal, this group registered no recurrence for a follow-up period of 2 years. Hietanen et al. did a comparative study of the efficacy of TAC (20 mg/mL) and 5-FU (50 mg/mL) in treating a total of 50 keloids by randomized control trial. In the follow-up period they documented efficacy for both measures are equal and registered a lower side effect for 5-FU treatment. Specifically, the combination

of 5-FU and TAC seems more effective than 5-FU or TAC alone. The ratios of 5-FU and TAC tried in different studies vary, even though ratios of 9:1 or 3:1 are most used protocols also show notable variation in the intervals between injections, between once weekly and every 4 weeks. Almost all the studies rely on rather subjective scales and few objective measurements. further, relatively some studies have tried long-term follow up periods. While most of the studies shows the combination of TAC and 5-FU has assured benefits, based on discussions among specialists in the field of scar/keloid management, it become apparent that the combination injection of a 3:1 ratio of 5-FU to TAC is becoming the most common procedure (M.Reinholz, A. G€urtler, H. Schwaiger, J. P€otschke, & G.G. Gauglitz, unpublished data).

We used ultrasound as a measuring technique to objectively find out changes in scar size, penetration depth and height to find out the efficacy of injecting a 3:1 ratio of 5-FU (50 mg/mL) and a crystalline TAC suspension (10 mg/mL) directly into keloid every 4 weeks. The 4ml volume was injected per patient, this reaches to a maximum dose of 150 mg 5-FU and 10 mg TAC per patient per injection. By this approach, the maximum dosage used is below the chemotherapeutic dose of 200–600 mg/m<sup>2</sup>.

In this study population of 30 patients, we were able to confirm that keloid volume and penetration depth reasonably decreased after four doses of injections with comparing baseline and 1-month follow-up results. These results stay stable till the 1-year follow up for most of the variables measured. All patients and the observer noted significant improvements throughout the entire study period. Notably, all patients show good improvements in their quality of life. This finding may be an important reason for more frequent consideration of this therapy in routine keloid management, as keloids are known to have a significant impact on affected patients' quality of life.

Along with a variety of studies have already showed that combinations of TAC and 5-FU may be superior to the respective monotherapies.

#### CONCLUSION:

The results of this study prove the efficacy and safety of the use of combination injection of 5-FU and TAC in a 3:1 ratio in keloids based on objective measurements. This treatment was tolerated well by the patient and yielding better results at 1-year follow up.

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