

Therapeutic effects of 5 fluorouracil in combination with crystalline triamcinolone acetonide suspension in treatment of keloids

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Abstract

Background: Keloids are benign hyperproliferations of dermal connective tissue. Injury of the deep dermis commonly results in scar formation. The present study was conducted to assess therapeutic effects of 5 fluorouracil in combination with crystalline triamcinolone acetonide suspension in treatment of keloids. **Materials & Methods:** 72 patients with keloids of both genders were treated with cryotherapy (spray cryotherapy using liquid nitrogen twice for 10 s; cryotherapy was usually performed 15–30 min before the injection of TAC) and TAC every 4 weeks at least three times without significant improvement. **Results:** Out of 72 patients, males were 40 and females were 32. Common site was chest in 20, shoulder in 12, back in 8 and all sites in 32. Previous therapy was TAP in 10, cryotherapy in 7 and laser therapy in 5. Dermatology Life Quality Index (DLQI) at baseline was 8.4, at 1 month was 2.8 and at 12 months was 2.4. Adverse effects were hyperpigmentation in 6, teleangiectasia in 2, ulceration in 1 and systemic side effects in 1 patient. The difference was significant ($P < 0.05$). **Conclusion:** The efficacy and safety of the combination of 5-FU and TAC in keloids found to be beneficial.

Key words: Keloids, Scar, Skin.

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Introduction

Keloids pose a significant challenge for treating physicians. A number of treatment regimens have been developed, such as the application of silicone-based products, cryotherapy or intralesional corticosteroids [1]. Keloids may affect large parts of the skin surface and lead to severe functional impairment, particularly in genetically prone patients. Keloids are benign hyperproliferations of dermal connective tissue. Injury of the deep dermis commonly results in scar formation [2]. The physiologic wound healing cascade consists of inflammation, proliferation, and a remodeling phase. In pathologic scar formation, a prolonged inflammatory phase and some molecular alterations concerning inflammatory pathways are held responsible for excessive scarring[3]. Keloids commonly appear on the upper trunk, and, in contrast to hypertrophic scars, which may show a similar appearance, they exceed the margins of the original wound. Keloids can occur spontaneously but often show a genetic predisposition[4].

Successful treatment using conventional means has proven difficult, with low rates of sustained responses and high relapse rates[5]. The commonly used glucocorticosteroid triamcinolone acetonide has many effects, including an anti-mitotic property inhibiting keratinocytes and fibroblasts and the suppression of tissue inflammation and vasoconstriction, resulting in keloid regression[6].

Whereas, 5-fluorouracil (5-FU) inhibits the proliferation of fibroblasts as a pyrimidine analogue and has been successfully used for the treatment of keloids for many years. Most studies have focused on demonstrating the effects of high-dose 5-FU therapy (40–50 mg/mL), while others have promoted a 'low-dose' therapy using 1.4–3.5 mg/mL of 5-FU[7]. The present study was conducted to assess therapeutic effects of 5 fluorouracil in combination with crystalline triamcinolone acetonide suspension in treatment of keloids.

Materials & methods

This study consisted of 72 patients with keloids of both genders. All were enrolled with their written consent. Demographic data such as name, age, gender etc. was recorded. Patients enrolled were treated with cryotherapy (spray cryotherapy using liquid nitrogen twice for 10 s; cryotherapy was usually performed 15–30 min before the injection of TAC) and TAC every 4 weeks at least three times without significant improvement. Routine blood tests with complete blood count, excluding pancytopenia, basic metabolic panel. Dermatology Life Quality Index (DLQI) was recorded at baseline, at 1-month and 12 months FU. Results were assessed statistically. P value less than 0.05 was considered significant.

Results

Table 1: Distribution of patients

| Total- 72 | | |
|-----------|-------|---------|
| Gender | Males | Females |
| Number | 40 | 32 |

Table 1 shows that out of 72 patients, males were 40 and females were 32.

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Table 2: Parameters in patients

| Parameters | Variables | Number | P value |
|---------------------------------------|-----------------------|--------|---------|
| Site | Chest | 20 | 0.04 |
| | Shoulder | 12 | |
| | Back | 8 | |
| | All sites | 32 | |
| Previous therapy | TAP | 10 | 0.09 |
| | Cryotherapy | 7 | |
| | Laser therapy | 5 | |
| Dermatology Life Quality Index (DLQI) | Baseline | 8.4 | 0.01 |
| | 1 month | 2.8 | |
| | 12 months | 2.4 | |
| Adverse effect | Hyperpigmentation | 6 | 0.03 |
| | Teleangiectasia | 2 | |
| | Ulceration | 1 | |
| | Systemic side effects | 1 | |

Table 2, Fig. 1 shows that common site was chest in 20, shoulder in 12, back in 8 and all sites in 32. Previous therapy was TAP in 10, cryotherapy in 7 and laser therapy in 5. Dermatology Life Quality Index (DLQI) at baseline was 8.4, at 1 month was 2.8 and at 12 months was 2.4. Adverse effects were hyperpigmentation in 6, teleangiectasia in 2, ulceration in 1 and systemic side effects in 1 patient. The difference was significant (P < 0.05).

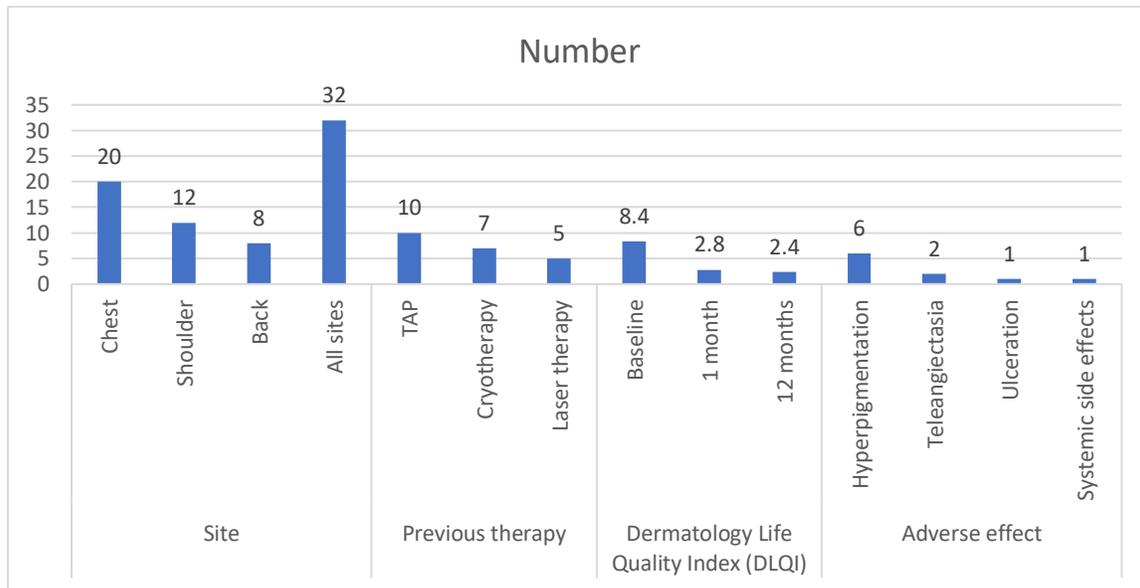


Fig 1: Parameters in patients

Discussion

New treatment options for keloid are intralesional injections of 5-fluorouracil, interferon, and bleomycin for therapy-refractory scars as well as non-ablative and ablative lasers[8]. In clinical practice, the injection of crystalline glucocorticoids alone or in combination with cryotherapy represents a well-proven therapy[9]. Combinational approaches seem to be superior than respective monotherapies. It is assumed that cryotherapy induces changes in microcirculation and apoptosis of fibroblasts in treated scars[10]. This procedure results in a localized dermal edema, which facilitates injections into the scar tissue as larger volumes can be applied more easily, thus enhancing the therapeutic effect[11]. Common side effects of cryotherapy are pain, a pro-longed healing time because of the induced blistering, and potential depigmentation. Triamcinolone acetonide reduces scar thickness by inhibition of the collagen biosynthesis and the proliferation of fibroblasts. Potential side effects include atrophy of the subcutis[12]. The present study was conducted to assess therapeutic effects of 5-fluorouracil in combination with crystalline triamcinolone acetonide suspension in treatment of keloids. In present study, out of 72 patients, males were 40 and females were 32. Schwaiger et al[13] evaluated the therapeutic benefits of

cryotherapy directly followed by intralesional crystalline triamcinolone acetonide injections using ultrasound and a 3D topographic imaging device. Fifteen patients with keloids were treated with cryotherapy and intralesional injections of triamcinolone acetonide for a total of 4 times at intervals of 4 weeks. Objective assessment was performed at each visit. After the last treatment, a significant average reduction of scar volume of 34.3% and an average decrease in scar height of 41.3% as determined by 3D imaging was observed compared with baseline. Ultrasound revealed an average reduction of scar height of 31.7% and an average decrease in tissue penetration depth of 37.8% when compared with baseline measurements. We observed that common site was chest in 20, shoulder in 12, back in 8 and all sites in 32. Previous therapy was TAP in 10, cryotherapy in 7 and laser therapy in 5. Dermatology Life Quality Index (DLQI) at baseline was 8.4, at 1 month was 2.8 and at 12 months was 2.4. Adverse effects were hyperpigmentation in 6, teleangiectasia in 2, ulceration in 1 and systemic side effects in 1 patient. Reinholtz et al[14] evaluated the therapeutic effect of four courses of intralesional 5-FU in combination with TAC (3 : 1) utilizing 3D analysis (PRIMOS), ultrasound and scar scales such as the Patient and Observer Scar Assessment Scales (POSAS) and the

Dermatology Life Quality Index (DLQI). Twenty-five patients with keloids were treated using 5-FU and TAC every 4 weeks. Objective assessments were performed and the scar scales administered at baseline, as well as during consecutive visits at 1- and 12-month follow-up (FU). Routine laboratory tests were performed at baseline and at 1-month FU. 3D PRIMOS and ultrasound measurements revealed highly significant and stable reductions in height (baseline mean score: 4.0 ± 1.7 mm, 1-month FU mean score: 1.5 ± 0.8 mm, 12-month FU mean score: 1.8 ± 0.9 mm, $P = <0.0001$), volume (baseline mean score: $1,105 \pm 911.5$ mm³, 1-month FU mean score: 416.1 ± 218.1 mm³, 12-month FU mean score: 431.2 ± 253.6 mm³, $P = <0.0001$, respectively) and penetration depth of keloids (relative reduction between baseline and 12-month FU of 74.4%, $P = <0.0001$). The POSAS and DLQI scales confirmed significant objective and subjective improvements in scar appearance in all categories. The life quality associated with keloid appearance improved from a 'moderate effect' to a 'small effect' throughout the course of the study.

Conclusion

Authors found that the efficacy and safety of the combination of 5-FU and TAC in keloids found be beneficial.

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