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Effect of intralesional injection of 5-Fluorouracil in Keloid: an observational study

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Abstract:

Background: Keloids are quite prone to recurrence. Although triamcinolone injections constitute current first-line treatment, it has been hypothesized that over half of keloids are steroid insensitive. **Aim:** The aim of this study is to evaluate the safety and efficacy of intralesional injection of 5-Fluorouracil in the treatment of keloids. **Hypothesis:** The hypothesis of the present study is that intralesional injection of 5-Fluorouracil is an effective and safe treatment option for keloids. **Materials & methods:** Over six months, fifty patients with sixty keloid scars underwent either intralesional triamcinolone or 5-fluorouracil injections. The remission rate at six months did not statistically differ between the 5-fluorouracil and triamcinolone groups—47% versus 61%, respectively, during the study period from February 2018 to January 2019. **Results:** In the triamcinolone group rather than the 5-fluorouracil group, local side effects were more pronounced. Skin atrophy occurred 45% in the triamcinolone group and 9% in the 5-fluorouracil group ($p<0.05$). Furthermore, occurring in the triamcinolone group was telangiectasia with a frequency of 51% and in the 5-fluorouracil 22% ($p<0.05$). **Conclusion:** In this investigation, triamcinolone and 5-fluorouracil injections had no difference in their clinical efficacy. For cosmetically sensitive skin areas, 5-fluorouracil injections could be better given the more negative effects noted following triamcinolone treatment.

Key words: Keloids, 5-Fluorouracil, Intralesional Injection, Dermatological condition, Topical medications, Triamcinolone.

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Introduction:

Keloids are a common dermatological condition that can cause significant physical and psychological distress. Keloids affect millions of people worldwide, and their treatment remains a significant challenge for dermatologists and other healthcare professionals [1,2]. Several treatment options are available for keloids, including surgery, radiation therapy, and topical medications [3]. Promising for keloids is 5-fluorouracil, a pyrimidine analog and antimetabolite [1]. Crucially important steps in keloid development, fibroblast proliferation and collagen synthesis are inhibited here [3]. By administering the medication straight into the keloid tissue, intralesional 5-fluorouracil provides a focused approach that maximizes local effects while reducing systemic exposure and related side effects [4]. The results might offer a basis for developing uniform treatment guidelines and raising patient care standards in dermatological practice. Despite these treatment options, keloids often recur, and there is a lack of consensus on the most effective treatment approach [6]. Intralesional injections are a minimally invasive treatment option that has shown promise in the treatment of keloids. What is the effect of intralesional injection of 5-Fluorouracil in the treatment of keloids? The aim of this study is to evaluate the safety and efficacy of intralesional injection of 5-Fluorouracil in the treatment of keloids. The hypothesis of the present study is that intralesional injection of 5-Fluorouracil is an effective and safe treatment option for keloids.

Materials & methods:

The study was approved by the Ethics Committee of the present study college and Hospital. At first, the outpatient clinic saw 100 patients with past-treated keloid scars. Enrolled and randomized into two groups, there were fifty patients in all with 60 active and symptomatic keloid scars needing therapy. We offered every patient the choice to enroll and provided them with advice on the research design. Patients who registered agreed to the trial following a first screening and a cooling-off period. There were some keloids treated for some patients undergoing treatment. We described a keloid as a scar that extends beyond the initial incision and shows no signs of healing for more than three years.

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This study encompassed any patient over the age of eighteen who was undergoing keloid treatment at our hospital and was suitable for receiving medication injections. The study excluded patients under the age of 18, those with pregnancy or intended pregnancy, lactation, renal failure, hepatic dysfunction, hematological disease or bone marrow suppression, and those with systemic or local infection.

Permuted-block randomization with closed envelopes ensured equal group sizes, resulting in two groups, each with 25 keloid scars. The senior author, a plastic surgeon, blindly selected each randomized choice of envelope; she also administered the drugs without disclosing the patient allocation—that is, drug treatment to the patients. Another plastic surgeon (the first author) evaluated the treatment reaction separately. Both the patient and the observer were blind during the evaluation of the outcome. The follow-up took place from February 2018 to January 2019. The plastic surgeon who performed the injections did not review any of the collected data.

Each patient received intralesional injections, either triamcinolone or 5-Fluorouracil. We saw all the patients for follow-up assessment five times in total—once every three to four weeks until week 12 and at six months.

The same senior plastic surgeon, who alone knew the outcome of randomization, administered the injections during the first three appointments. We followed the recommended guidelines for the injections. We injected either triamcinolone or 5-Fluorouracil into the keloid under local anesthesia, taking great care not to inject under the keloid mass or too close to the epidermis to avoid unnecessary local side effects. The injection technique was equal, as stated in earlier works. We kept the injection in the scar until blanching occurred. We performed control visits without additional injections for patients who responded well and did not require three injections. We randomly divided the patients into two groups and administered either triamcinolone or 5-Fluorouracil injections, without any placebo injections.

For triamcinolone injections, 20 mg/ml combined 1:1 with lidocaine 10 mg/ml (Orion Pharma, Finland). We used Five-fluorouracil at a 50 mg/ml concentration for 5-Fluorouracil injections. Lidocaine provided the first local anesthetic for both groups. Hospital pharmacies manufacture 5-Fluorouracil, which is cytostatic and incompatible with lidocaine. However, we can consistently

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administer triamcinolone in conjunction with a local anesthetic, which is why we did so. The first author, a blinded observer, evaluated the keloids using the established scar scale, the Patient and Observer Scar Assessment Scale (POSAS), and conducted an objective assessment using a Spectro cutometer camera. We investigated the keloids for indications of telangiectasia and skin atrophy. At every appointment, every patient completed a component of the POSAS scale related to their condition. Spectro cutometer enabled the computation of the keloid's estimated hemoglobin concentration, as previously reported.

The main goal of the study was to see if the keloid went away six months after treatment. Other goals were the POSAS score, local side effects, blood vessel density, an estimated change in hemoglobin concentration, and fibroblast proliferation. Clinically, the blinded observer described the keloid's remission as flattening to the degree where no more injections were practical or necessary. The same blind observer reached conclusions about potential side effects, skin atrophy, and telangiectasia.

Statistical analysis:

SPSS version 21.0 tools IBM SPSS Statistics were used. The chi-square (discrete variables) test and Mann-Whitney U test (continuous variables) were applied for a comparison of patient features between the triamcinolone and 5-Fluorouracil groups. With a chi-square test, the frequency of adverse effects was investigated. Calculations were paired t-test comparisons between the baseline and post-treatment data. Considered statistically significant was a P-value smaller than 0.05.

Results & Discussion:

Over six months, fifty patients with sixty keloid scars underwent either intralesional triamcinolone or 5-fluorouracil injections. The remission rate at six months did not statistically differ between the 5-fluorouracil and triamcinolone groups—47% versus 61%, respectively. In the triamcinolone group rather than the 5-fluorouracil group, local side effects were more pronounced. Skin atrophy occurred at 45% in the triamcinolone group and 9% in the 5-fluorouracil group ($p<0.05$). Furthermore, telangiectasia occurred in the triamcinolone group with a frequency of 51%, and in the 5-fluorouracil group, 22% ($p<0.05$). Triamcinolone injections have been a standard procedure

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for treating keloids for a long time [7-9]. Even though studies have published patients treated with 5-fluorouracil alone, the effects of 5-fluorouracil treatment on keloid scars remain experimental, despite the limited number of randomized controlled studies that have examined this approach. Both of these experiments came back with good results—a 70–95% success rate. Neither of these studies, though, were randomized controlled trials. A study performed a randomized controlled experiment comparing 5-fluorouracil and triamcinolone injections [12]. Their investigation followed ours in terms of sample size, injection rate, concentrations, and dosages applied.

A study [12] assessed general progress. The observer's patient reports of outcome and assessment showed that 5-fluorouracil injections yielded noticeably better results than triamcinolone ones. In the present investigation, the two therapies' efficacy did not show any appreciable variation. The triamcinolone and 5-fluorouracil groups both responded favorably, and both groups showed a statistically significant change between baseline and 6 months. Compared to previous studies discussed above, less than half of the patients in this trial were in remission following 5-fluorouracil treatment, despite the fact that 5-fluorouracil injections had a notable impact.

In our study, local side effects were more frequent in the triamcinolone group than in the 5-fluorouracil group. Previous studies, too, have recorded negative effects from triamcinolone injections. While a study [9] reported ulceration in 21.4% and burning sensation in 7.1% at the 5-fluorouracil treatment sites, another study [12] recorded no adverse effects in either group. However, other studies linked triamcinolone therapy to notable local side effects. Reporting their experiences with 5-fluorouracil injections for hypertrophic scarring, studies noted neither systemic nor local side effects [13, 14]. Conversely, a study [8] found that 30% of their patients showed superficial ulcers in their keloids following 5-fluorouracil injections, and all 20 of their patients claimed the injections were unpleasant. According to the same study, patients had hyperpigmentation at the treatment sites; this did not result in any appreciable cosmetic morbidity and finally disappeared [15]. A study investigating triamcinolone, 5-fluorouracil, and their combination in keloid therapy [16] was conducted in randomized parallel group research. Although triamcinolone, 5-fluorouracil, and their combination are all successful in keloid treatment, the combined treatment of triamcinolone and 5-fluorouracil was superior in efficacy and incidence of side effects [16, 12]. Sadeghinia et al. found skin ulcers in patients in the 5-

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fluorouracil group [16]. Contrary to what they found, our side effect profile was minimal. One patient in our trial experienced a local allergic reaction and skin blistering following the second 5-fluorouracil injection, therefore ending the treatment. We don't know why this occurred or if the cytotoxic action caused the ulceration.

In the 5-fluorouracil group, three patients had hyperpigmentation. The triamcinolone group showed significantly more skin atrophy, 51% telangiectasia, and 45% local adverse effects, compared to 9% and 22% in the 5-fluorouracil group, respectively. This observation could help to explain the function of 5-fluorouracil over triamcinolone, particularly in cosmetically important locations where local adverse effects could cause significant aesthetic difficulties. Still, this small study does not allow one to draw a firm conclusion. More participants in this study would be required to provide a more realistic side effect profile. Another study contrasting triamcinolone with 5-fluorouracil could shed some light on the additional efficacy combinatorial therapy could bring.

We used a spectrocutometer to show that triamcinolone injections may lower the vascularity of a keloid by lowering the density of the blood vessels and estimating the amount of hemoglobin in the keloid.

Our study's short six-month follow-up period is insufficient to track for keloid recurrence, which can strike as late as twenty-four months or more following therapy.

More modes of evaluation would have strengthened this investigation; nevertheless, we do offer some preliminary data indicating the similar but rather similar effectiveness of triamcinolone and 5-fluorouracil. After three to four injections, these treatments often show some effect; nonetheless, should no response be observed, it is advised against carrying on with the same line of therapy. Patients from this trial underwent surgery and radiotherapy, but benefits were absent; some also had additional substance injections (triamcinolone or 5-fluorouracil) and pressure garments or

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silicone gel sheeting. This small study aims to compare triamcinolone and 5-fluorouracil as early minimally invasive therapy modalities, rather than disputing the efficacy of other thoroughly investigated modalities.

Conclusion:

In this investigation, triamcinolone and 5-fluorouracil injections had no difference in their clinical efficacy. For cosmetically sensitive skin areas, 5-fluorouracil injections could be better given the more negative effects noted following triamcinolone treatment. Future studies could explore the long-term efficacy and safety of intralesional 5-Fluorouracil injections in a larger, multicenter trial, as well as investigate potential biomarkers for predicting treatment response in keloid patients.

Conflict of interest:

There is no conflict of interest among the present study authors.

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