Research Article

Effective Treatment of Keloids with Three-Dose Moderate-Strength Intralesional Triamcinolone Acetonide (TAC) Regimen

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Abstract

Introduction: The most devastating consequence of any injury is scar formation. Among all the surgical specialties, plastic surgery faces the worst dilemma as patients expect it to be the scar-less surgery.

Objectives: This study aims to set an effective dose of triamcinolone acetonide intralesional injection to achieve successful results in the treatment of keloids.

Methods: A prospective interventional study was conducted in the Department of Plastic Surgery, Shaikh Zayed Hospital Lahore for 2 years. Triamcinolone acetonide was injected intralesional at a dose of 4mg/cm2 every 4th week. . The improvement in scar appearance, pain, and itch were measured using Vancouver Scar Scale (VSS), Visual Analog Scale (VAS), and the St Andrew's itch egg scale, respectively up to 12 months of therapy.

Results: Among the 40 patients, 12 were males and 28 were females. The mean age of patients was 32.8 years and the most common sites were the chest, earlobes, and back. There was a substantial progressive improvement in VSS and VAS scores over one year. A significant reduction in pruritus was also observed in the patients. No recurrence was noted at the end of 12 months.

Conclusions: A moderate-strength dose of 4mg/cm2 as a single intralesional injection of triamcinolone acetonide every four weeks is effective in decreasing the size of keloids and relieving the symptoms such as pain and itching.

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Introduction

The most devastating consequence of any injury is scar formation. Among all the surgical specialties, plastic surgery faces the worst dilemma as patients expect it to be the scar-less surgery. Keloids and hypertrophic scars add an extra challenge for management as they have been most troublesome when it comes to achieving good functional and cosmetic outcomes.

A hypertrophic scar is thick and raised which often develops after an abnormal response to injury.[1] It is often cosmetically and functionally displeasing. Hypertrophic scars sometimes regress with time[2] Keloids are even worse than hypertrophic scars as they grow beyond the margins of the initial injury site or wound and are asso-

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ciated with more bothersome complaints like pain and itching than hypertrophic scars and they never regress on their own. They are cosmetically and functionally more disfiguring and are more difficult to manage than hypertrophic scars. Keloids differ from hypertrophic scars also on a histological basis. Keloids, mainly, contain thick bundles of type 1 and type 3 collagen fibers, which are irregularly branched and have septal disorganization with an excess of myofibroblasts and are without nodules.[3]

Various treatment options have been proposed to manage hypertrophic scars and keloid i.e. both surgical and nonsurgical. These include excision with or without skin grafts especially for hypertrophic scars, pressure garments,[4] intralesional bleomycin[5], intralesional steroids,[6] and laser therapy[7] among many others. All these treatments have variable success rates.

Intralesional steroids have been the first line of therapy for the management of keloids for many decades.[8] Triamcinolone acetonide (TAC) is the most commonly used intralesional steroid for keloids. It has been used alone or in combination with other drugs. Various formulations and dosage regimens have been recommended for intralesional injection administration. The purpose of our study is to evaluate a three-dose moderate-strength dosage regimen of intralesional triamcinolone acetonide injection for keloids in terms of improvement in scar appearance, pain and pruritus. The results will help the clinicians to set an effective dosage regimen of I/L TAC injection for the successful management of keloid scars.

Methods

A prospective interventional study was conducted in the Department of Plastic Surgery, Shaikh Zayed Hospital Lahore for a period of 24 months starting from June 2019 to June 2021. This study included patients in the age group of 15-65 years, with keloids ≤ 10cm^2. Patients with keloids > 10cm^2 in size, showing no response after 2nd dose, having hypersensitivity to triamcinolone, connective tissue disorders, pregnancy, and lactation were excluded from the study. A detailed history of the duration, etiologic factors, prior treatment, and evidence of any significant systemic disease was obtained. Written informed consent was taken from all patients.

The details of the scar were noted in terms of length and width measured in centimeters using a Vernier caliper. The scars were scored initially before starting the treatment utilizing the Vancouver Scar Scale (VSS) which ranges from 0 (best possible scar) to 13 (worst possible scar). The pain was recorded using the Visual Analog Scale (VAS) for a range of 1 to 10, with 1 being the minimum and 10 as the maximum. Pruritus was assessed using the St Andrew's itch egg scale (0 to 4), with 0 having no itch and 4 being graded as severe itch.

Injection of triamcinolone acetonide at a concentration of 40mg/ml was used. After a negative skin hypersensitivity test, the lesion was anesthetized with local anesthesia by using 2% lignocaine. Then triamcinolone was injected intralesional with an insulin syringe at a dose depending on lesion size (4mg/cm^2). The TAC injections were scheduled at 4-weekly intervals for three consecutive months and a maximum of 3 injections were given.

All the patients were followed up at monthly intervals after the three doses of triamcinolone infiltration for up to 3 months and then 3-monthly afterward. On every visit, the appearance of the scar, pain, and pruritus were recorded. The final assessment was done after 12 months of therapy.

A proforma was designed to collect all the data. Patients' demographic particulars (age, gender, addresses, and contact numbers), size and site of keloids, dates of 1st, 2nd, and 3rd doses of intralesional TAC injection, VSS scores, VAS scores, St Andrew's Itch Egg scores, complications and recurrence (if any) were recorded.

Statistical Package for the Social Sciences program (SPSS) Ver. 23 was used for statistical analysis. Age, the average size of keloids, VSS scores, VAS scores, and St Andrew's Itch Egg scores were described in mean ± standard deviation (SD). Data for gender, site of keloids, and complications were expressed in terms of frequency and percentages.

Results

Initially, 83 patients fulfilled the selection criteria for the study. Of these, 40 patients i.e. 28 females and 12 males were available for analysis at the end of the study. 7 patients didn't complete the course of three injections, 2 patients became pregnant, 11 patients were lost to follow-up and 23 patients showed no response after 2nd dose. The mean age was 32.8 ± 5.4 years and the average size of the keloids was 8.3 ± 1.7cm^2. The most common

site was the chest followed by the earlobe and back. (Table 1)

There was an improvement in VSS and VAS scores following the first injection which was progressive throughout the treatment. A mean improvement of 5.88±2.16 (62.02%) and 3.52±1.77 (60.38%) was noted at the end of the treatment in VSS and VAS scores, respectively. Paired t-test for the statistical analysis showed that the difference at 12 months was significant (<0.0001) for both appearance and pain. Most of the patients complained of pruritus which improved over a period with a significant difference in itch score (p=0.0068) at 12 months. (Table 2) (Figure 1)

No recurrence was noted at the end of 12 months. However, skin ulceration was observed in 2 patients and only 1 patient reported hyperpigmentation. In addition, skin thinning was recorded in 4 patients. (Table 3)

Table 1: *Demographic Data*

Mean Age		**32.8 ± 5.4 years**
Gender	Male	12 (30%)
	Female	28 (70%)
Average Size of Keloids		8.3 ± 1.7cm^2
Site of keloids		
• **Chest**		18 (45%)
• **Earlobe**		14 (35%)
• **Back**		08 (20%)

Table 2: *Keloid Assessment Scores*

Parameters	**Before treatment**	**After treatment**	**Mean Improvement**		**P-value**
	Mean±SD	Mean±SD	Mean± SD	Percentage	
Appearance Vancouver Scar Scale	9.48±1.8	3.6±1.21	5.88±2.16	62.02%	<0.0001
Pain Visual Analogue Scale	5.83±1.37	2.31±1.12	3.52±1.77	60.38%	<0.0001
Pruritus St Andrew's Itch Egg	3.21±2.11	2.08±1.47	1.13±2.57	35.20%	0.0068

Table 3: *Complications*

Skin Ulceration	2 (5%)
Hyperpigmentation	1 (2.5%)
Skin Thinning	4 (10%)

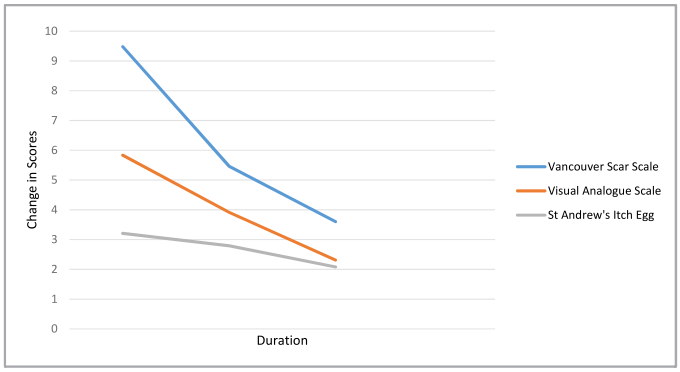

Figure 1: *Trends in the Appearance, pain and Itch of Keloids with Intralesional Triamcinolone Acetonide Injections*

Discussion

Keloids represent an abnormal healing response and have become a management challenge for clinicians. Patients at high risk of keloids are young, with a genetic tendency, and have darker skin. The most notorious areas for the development of keloids are pre sternal, earlobes, helical rims, and shoulders.[9]

Keloids are usually raised hyper-pigmented scars that grow beyond the margins of the original wound and never regress. The word keloid has originally derived from the Greek word *cheloides* meaning "crab's claw".[10] Keloids primarily result from an abnormal wound healing process that occurs due to a lack of control mechanism which regulates the proliferation of cells and ultimately tissue repair.[11] Histologically, keloids are mainly made up of hyalinized collagen bundles which are randomly arranged and have a tongue-like projection entering into the papillary dermis.[12] No specific gene has been associated with the development of keloids till now, however, various genes are postulated to be responsible for the development of keloids in various families.[13,14]

Keloids are characterized by excess deposition of the extracellular matrix resulting from an increased rate of fibroblast proliferation and decreased rate of their degradation.[15,16] Despite various clinical trials and experimental studies, the exact pathological mechanisms contributing to the development of keloids have not been completely identified. Keloid fibroblasts have been identified to have high levels of PAI-1 and low levels of urokinase which may be attributed to decreased rate of collagen degradation.[17,18] Several other theories have been suggested but the exact mechanism is still

unknown.

As with the pathological mechanism of keloids, the management faces the same dilemma as multiple treatments have been recommended and used but none of them has cured the keloids effectively. Various treatment options include pressure therapy,[4] silicone gel sheet application,[19] intralesional injections of triamcinolone,[17] interferons,[20] bleomycin,[21] 5-florouracil[15], and verapamil,[22] onion extract gel application,[23] laser therapy,[7] radiation,[2] intralesional needle cryosurgery,[24] and surgical excision.[15, 20] Amongst all, the most widely used and recommended is the use of intralesional steroids either alone or in combination with various other drugs and modalities.[2,15]

Intralesional steroids have been in use for the treatment of keloids and hypertrophic scars for decades[8] but their exact mechanism of action has not been understood yet. This lack of understanding is the main reason for the variability in the results and dose regimens used by various centers to treat keloids.

Steroids induce regression of keloids through different pathways including suppression of the inflammation by inhibition of chemotaxis and phagocytosis, and reduction in oxygen supply by steroid-induced vasoconstriction. Reportedly, steroids have an inhibitory effect on keratinocytes and fibroblasts which reduces re-epithelialization as well as collagen deposition and promote collagen degradation by reducing plasma protease inhibitors. Various secondary mechanisms have also been postulated like a decrease in alpha-1 antitrypsin levels and decreased levels of TGF-B and IGF-1. All these pathways tend to affect the overall growth and pathogenesis of keloids.[25,26]

Besides the ambiguity in the actual mechanism of action of steroids on keloids, there is no consensus on the standard dosage regimen and time duration for the therapy. Several dosage regimens ranging from 2mg/cm^2 to 10-20 mg/ml, different frequencies of injection for treatment i.e. one injection weekly to one injection monthly, and various duration ranging from a total of four injections to eight injections have been reported in the literature.[17,22,26]

The use of intralesional steroids has also been associated with some local and systemic complications including skin and subcutaneous tissue atrophy, ulceration, hypopigmentation, telangiectasia, and Cushing syndrome.[27] The risk of local complications is greater than systemic complications and is directly related to the dose of injection and the technique of administration.

In this study, we have tried to eliminate the aforementioned problems and set a standard dosage regimen and duration of treatment for efficient results. We have elected our dosage based on the surface area of the lesion and the total duration of treatment was limited to three injections maximum. Hence, we have discovered that maximum results were obtained with three injections and no further injections were required. However, patients were followed up at regular intervals for any signs of recurrence or complications.

In our study, we found that the use of a standard dose of 4mg/cm^2 as a single injection every four weeks is quite effective in reducing the growth of keloids and relieving the symptoms such as pain and itching. A significant mean reduction in VSS i.e. 62.02% was observed, which is in concordance with the results of other studies.[28,29] In addition, a significant decrease in the pain and itch scores was noted, which is relatable to the research works by Ghai et al[30] and Belie et al.[31]

Since the dose was carefully calculated according to the surface area, the complication rate was quite low. Only two patients suffer partial skin ulceration in which the treatment was stopped and the wound was managed conservatively. Partial hypopigmentation was seen in some patients which resolved with time. No actual hypotrophy of the surrounding area or any systemic complications were seen. These observations are comparable to that of Garg AM et al.[28]

Conclusion

A moderate-strength dose of 4mg/cm^2 as a single intralesional injection of triamcinolone acetonide every four weeks is effective in reducing the growth of keloids and alleviating the symptoms such as pain and itching.

Ethical Approval: The study was approved by Ethical Committee Shaikh Zayed Medical Complex Lahore vide letter no. Ref.SZMC/PS/09/20.

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Authors' Contribution:

TN: Study concept & design, writing manuscript

JF: Study design, data collection, data analysis, writing manuscript

MARM: Literature search, data interpretation

SNJ: Proof reading of manuscript

AU: Data collection & helped in manuscript writing

SA: Data collection & helped in manuscript writing

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