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Original Article

Comparison of Efficacy of Intralesional Triamcinolone Versus Combination of Triamcinolone with 5-Fluorouracil in The Treatment of Keloid

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ABSTRACT

Objective: To study the efficacy of intralesional Triamcinolone versus combination of Triamcinolone with 5-Fluorouracil in the treatment of keloid in terms of reduction in height of lesion.
Study Design: Quasi-experimental study.
Place and Duration of Study: Department of Plastic Surgery, Combined Military Hospital, Rawalpindi Pakistan, Jul 2020 to Mar 2021.
Methodology: A total of 56 patients suffering from keloid formation were included in our study. Patients who had received previous treatment for keloids were excluded. All patients were assessed for volume of keloid before and after 8 weeks of intervention. Group-A patients received therapy with intralesional Triamcinolone 4 mg with 5-Fluorouracil 45 mg once weekly while Group-B patients received intralesional Triamcinolone 10 mg alone once weekly. Patients were followed up after 8 weeks to ascertain mean reduction in volume of keloid post-intervention.
Results: The difference in total volume post-treatment between the two groups was statistically significant, however, the difference in total volume reduction across both groups with treatment was not statistically significant. Treatment was effective in 23(82.1%) patients with the combination of Triamcinolone and 5-Fluorouracil, while only 16(57.1%) responded to treatment with Triamcinolone alone.
Conclusion: The combination of intralesional Triamcinolone and 5-Fluorouracil is superior to intralesional Triamcinolone alone in the treatment of keloids.

Keywords: 5-Fluorouracil, Keloid, Triamcinolone

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INTRODUCTION

Keloids are the result of defects in wound healing, occurring at the site of a dermatological injury that extend beyond its borders over time, tending to occur in darker-skinned individuals with an estimated global incidence of 5–16%, occurring equally in both genders.[1] The formation of a keloid occurs as a result of a disequilibrium between the deposition of collagen and the extracellular matrix versus its removal, due to over-stimulation of fibroblasts via an increased production of Transforming Growth Factor (TGF) β1 and β2, as Keloid fibroblasts are exceptionally sensitive to these stimuli due to receptor up-regulation.[2,3] Keloids can occur in any scar and are notoriously difficult to manage as they respond poorly to treatment and may worsen following inadequate therapy, which is mostly prevention, where susceptible patients are advised to avoid elective procedures and, where unavoidable, trauma to the skin is kept to a minimum. Quick wound closure, complete hemostasis, and decreased wound tension also help to reduce incidence.[4] Compression therapy is helpful up to varying degrees.[5,6] Other treatment modalities include intralesional steroids, cryotherapy, surgical excision, radiotherapy, laser therapy, topical imiquimod, intralesional Botox, intralesional bleomycin, intralesional 5-fluorouracil, and silicone gel sheeting.[7] Intralesional Triamcinolone is a first-line therapy associated with a varying degree of success as its therapeutic effect is attributed to the direct inhibition of fibroblast activity and their recruitment, due to which it has been used as mono-therapy and in conjunction with other treatment methods.[8] 5-fluorouracil has been relatively recently employed in the treatment of keloid and is used as an adjunctive treatment.[9] Multiple studies have been conducted into the role of both drugs and their combination in the treatment of keloids but the results have been inconclusive.[10]

Keloids are a relatively common problem which results in significant distress to the patient, especially

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with regards to pain and cosmetics. While many modalities have been used to manage keloids, an effective treatment remains elusive. Thus, this study was conducted to determine the role of corticosteroids as first line therapy as well as that of combination therapy with corticosteroids and 5-Fluorouracil.

METHODOLOGY

The quasi-experimental study was conducted from July 2020 to March 2021 at the Department of Plastic Surgery, Combined Military Hospital (CMH), Rawalpindi, Pakistan, after obtaining ethics clearance from institutional Ethics Review Board via IERB letter number 188/07/21. We enrolled 56 consenting patients diagnosed with keloid formation, chosen via non-probability consecutive sampling. The WHO sample size calculator was used to calculate the sample size and anticipated population mean of 1.894.[11]

Inclusion Criteria: Patients of either gender, between the ages of 15-80 years, with at least one keloid greater than 1 cm. were included.

Exclusion Criteria: Patients who were pregnant or lactating, had received previous intralesional treatment for keloid, had history of liver or kidney dysfunction or were suffering from any form of immune deficiency, were excluded.

All patients were thoroughly evaluated by history and clinical examination on enrollment in the study. Patients were divided into two equal groups of 28 patients each by lottery method. All patients were assessed for length, width and height of the keloid before administration of treatment. Group-A patients received therapy with intralesional Triamcinolone 4 mg with 5-Fluorouracil 45 mg once weekly while Group-B patients received intralesional Triamcinolone 10 mg alone once weekly (Figure). Both groups received treatment for a total of 8 months. A 25-gauge needle was injected into different parts of the lesion till blanching was observed, each prick was separated from the others by 1 cm. All lesions were assessed at the end of treatment using photographs documenting the length, width and height of the lesion. A treatment was said to be efficacious if there was a reduction in volume of initial keloid size.

Data was analyzed using Statistical Package for the Social Sciences (SPSS) ver 26.0. Mean±SD was calculated for quantitative variables like age, dimensions of lesion (both before and after treatment), volume of lesion both before and after treatment, and reduction in volume of lesion. Qualitative variables like gender, location of keloid and whether the initial skin wound was traumatic or surgical were recorded in terms of frequency and percentage. Chi square test and independent samples t test was applied with the *p*-value of ≤0.05 being considered significant.

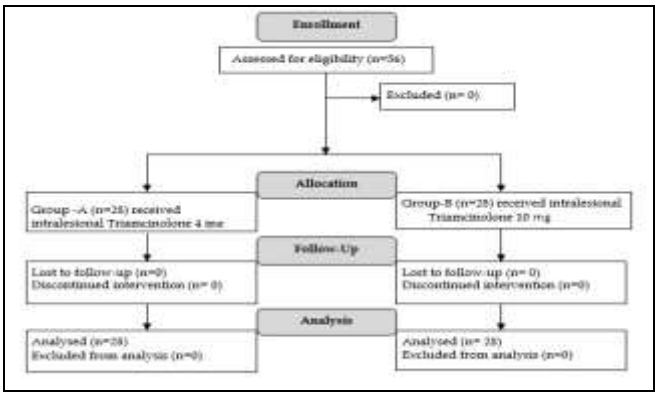

Figure: Patient Flow Diagram (N=56)

RESULTS

We studied a total of 56 patients with mean age of 48.50±14.16 years. A total of 26(46.4%) patients suffered from keloid involving the head and neck, 22(39.3%) had chest involvement while the abdomen and lower limbs were involved in 4(7.1%) cases each. In 42(75%) patients, the initial insult was the result of trauma while 14(25%) resulted from surgical incisions. Pre-treatment patient characteristics and their comparison across both groups is shown in Table-I.

Table-I: Patient Characteristics Pre-Treatment

Variable	Group A	Group B	*p*-value
Gender			
Male	7(25.0%)	10(35.7%)	0.383
Female	21(75.0%)	18(64.3%)	
Age (years)	48.54±14.36	48.46±14.21	0.985
Location of Keloid			
Head and Neck	12(42.9%)	14(50.0%)	0.597
Chest	13(46.4%)	9(32.1%)	
Abdomen	2(7.1%)	2(7.1%)	
Lower Limbs	1(3.6%)	3(10.8%)	
Initial Insult			
Traumatic	19(67.9%)	23(82.1%)	0.217
Surgical	9(32.1 %)	5(17.9%)	

The characteristics for keloids in both groups, both pre- and post-treatment, are shown in Table-II. The difference in total volume pre-treatment between the two groups was not statistically significant, but this became statistically significant post-treatment however it must be noted that the difference in total volume reduction with treatment was not significant

between the two groups. Treatment was seen to be efficacious in 82.1% of Group A, while this figure was only 57.1% in Group B.

Table-II: Keloid Characteristics Pre- And Post-Treatment

Variable	Group A	Group B	*p*-value
Pre-treatment Keloid Characteristics			
Length (cm)	12.20±6.64	11.61±6.45	0.739
Width (cm)	4.93±2.22	5.00±2.39	0.908
Height (cm)	1.87±1.03	2.14±1.12	0.361
Volume (cm+)	127.18±140.88	138.04±163.45	0.791
Post-treatment Keloid Characteristics			
Length (cm)	7.63±3.98	8.82±4.89	0.321
Width (cm)	3.65±2.13	6.52±2.74	<0.001
Height (cm)	1.08±0.46	1.36±0.47	0.027
Volume (cm3)	30.38±29.56	74.37±59.61	0.001
Volume Reduction (cm)	96.79±141.12	63.67±140.04	0.382
Treatment Outcome			
Success	23(82.1%)	16(57.1%)	0.042
Failure	5(17.9%)	12(42.9%)	
Complications	-	-	1.0

DISCUSSION

Our study demonstrated that the combination of intralesional Triamcinolone and 5-Fluorouracil was more effective in the management of keloids than Triamcinolone alone in terms of reduction in volume of lesion, with specific improvements in height. Previous studies conducted on the subject lacked clear protocols on blinding and randomization which we tried to overcome in this study.[12-15] Our study sample was comprised of a majority female population similar to Darougheh *et al*. who also encountered a predominantly female population.[12] while Khan *et al*. reported a more balanced population.[13] Female preponderance may be attributed to the fact that keloid is proposed to be more common in this gender.16 The mean age of our sample was 48.50±14.16 years, while this was 24.3±9.95 years and 29.45±9.29 years in Darougheh *et al* and Khan *et al*, respectively.[12,13] This difference may be as a result of different ethnicities, environmental factors and sun exposure in the study populations.[3]

Keloids are difficult to manage and numerous treatment regimens have been proposed for its management including both conservative and surgical methods.[17] Intralesional corticosteroids such as Triamcinolone are recognized as first line treatment for keloids18 however, it must be noted that the efficacy of Triamcinolone has been reported to be highly variable, with reported successful treatment of keloid rates ranging between 51% and 100%, making it unsatisfactory.[19] Moreover, being a potent corticosteroid, Triamcinolone is associated with adverse effects such as formation of telangiectasias, altered skin pigmentation at injection site and steroid associated skin atrophy.[20] 5-Fluorouracil in monotherapy has been demonstrated to be effective intralesional for keloids, with negligible systemic side effects, however, it is associated with local side effects such as pain, erythema, increased pigmentation and, in extreme cases, ulceration.[21] Our study sample did not show any adverse effects in either study arm. Darougheh *et al* reported a 37% complication rate with triamcinolone alone, while there were no complications seen in the combination therapy arm.[12] Khan *et al*. reported a24% complication rate with Triamcinolone alone, and an 8% rate with combination therapy.[13] Triamcinolone has been documented to reduce local inflammation caused by 5-Fluorouracil, reducing the incidence of side effects.[22] This was in-line with our study, however Davidson *et al*.[23] reported a total adverse effect rate of 23% with combination therapy versus 15% with steroid alone, which we did not encounter. Triamcinolone alone is known to have a rate of recurrence ranging between approximately 9 to 50%24, similar to the recurrence rate with the combined regimen, which is estimated to be around 17.5%.[11] Kontochristopoulos *et al*.[25] reported a success rate of 85%, similar to our figure of 82.1%. Conversely, Darougheh *et al*.[12] reported a success rate of 55% in their study for combination therapy, and 20% for Triamcinolone alone, both which were lower than in our study. While the results of this study are encouraging, it must be emphasized that the best treatment for keloid is prevention and utmost care must be taken in patients who have previous history of keloid formation, or who are known to be susceptible, when carrying out surgical procedures. This remains the best way to reducing morbidity and improving quality of life when dealing with keloids.

LIMITATIONS OF STUDY

Our study was limited by the duration of follow up. In addition, there was a requirement for further study of this regimen with regards to long-term outcome, specifically its side effects and rate of recurrence of keloid.

CONCLUSION

Triamcinolone and 5-Fluorouracil have been demonstrated to be useful for the treatment of keloid with impressive improvement rates, with a concurrent decrease in local side effects.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SF & SH: Conception, study design, drafting the manuscript, approval of the final version to be published.

AM & AA: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

SA & MAN: Data acquisition, critical review, approval of the final version to be published.

the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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