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Original Article

Comparison of efficacy of intralesional 5-Flourouracil plus triamcinolone acetonide verses intralesional triamcinolone acetonide alone in the treatment of keloids

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Abstract

Background Keloid is a benign well demarcated area of dense, fibrous tissue overgrowth that extends beyond the original defect. It is a result of an overgrowth of granulation tissue at the site of a healed skin injury. A variety of treatment regimens have been used for the management of keloids but none proved satisfactory.

Methods A total of 150 patients (75 in each group), fulfilling inclusion and exclusion criteria, were included in the study after taking informed consent. Local anesthesia was given in the form of injection lignocaine sublesionally in both groups. In group A, injection 5-flurouracil 10mg/ml (0.2ml) plus triamcinolone acetonide 10mg/ml (0.25ml) was given intralesionally, 2mm apart. In group B, injections triamcinolone acetonide 10mg/ml (0.25ml) alone was given intralesionally, 2mm apart. These injections were repeated after 3 weeks in each group for a duration of 3 months. Photographs were taken at base line and the end of 14th week. Efficacy was measured in terms of >75% reduction in size of keloids (measured by a dialed caliper) from baseline till the end of 14 weeks.

Results Efficacy was achieved in 55% (n=43) of patients in group A and was achieved in 36% (n=27) of patients in group B. The difference in efficacy of both groups was statistically significant with p value of 0.00.

Conclusion We concluded that the efficacy of intralesional 5-flurouracil plus triamcinolone acetonide is significantly higher than intralesional triamcinolone acetonide alone for the treatment of keloids.

Key words
Keloid, 5-Flurouracil, triamcinolone acetonide.

Introduction

Keloids are a common problem with a reported incidence of 4.5 to 16 percent in darker-skinned individuals. Keloid is a type of scar which, depending on its maturity, is composed mainly of either type III (early) or type I (late) collagen. It is a result of an overgrowth of granulation tissue at the site of a healed skin injury which is then slowly replaced by collagen type I. Keloids are firm, rubbery lesions or shiny, fibrous

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nodules, and can vary from pink to flesh-colored or red to dark brown in color. A keloid scar is benign, non-contagious, but sometimes accompanied by severe itchiness, pain and changes in texture. In severe cases, it can affect movement of skin.[1,2]

They are more common in darker skin types and in specific anatomic sites such as the chest, upper back, and shoulders.[3,4] Several types of injury, including surgery, piercings, burns, lacerations, abrasions, tattooing, vaccinations, insect bites, and inflammatory processes, such as acne, varicella, and folliculitis, can produce keloids.[3]

Keloids are found only in humans and occur in 5-15% of wounds. They tend to affect both sexes equally. The frequency of keloid occurrence in persons with highly pigmented skin is 15 times higher than in persons with less pigmented skin. The average age at onset is 10-30 years. Persons at the extremes of age rarely develop keloids.[5]

Some evidence supports a relationship between genetic predisposition and an individual's propensity to form keloid scars. Genetic associations for the development of abnormal scars have been found for HLA-B14, HLA-B21, HLA-BW16, HLA-BW35, HLA-DR5, HLA-DQW3, and blood group A.[6]

Various treatment options are available for painful or cosmetically disfiguring keloids including excision, intralesional steroid, intralesional 5-Fluorouracil (5-FU), intralesional 5-FU with steroid, silicone gel sheeting, cryosurgery, compression therapy, radiation therapy, interferon alfa, surgery, intralesional verapamil, Laser therapy and imiquimod.[4,7,9]

Intralesional steroid has traditionally been the mainstay of treatment for keloids. The most commonly used corticosteroid is triamcinolone acetonide (TAC). Intralesional TAC administration has shown clinical efficacy. However, there are a significant number of treatment failures and substantial inconsistencies with regard to the reproducibility of results.[4] Additionally, adverse effects including hypopigmentation, atrophy, and telangiectasias have been reported to be as high as 37% in the literature.[8]

Routinely intralesional TAC alone is used for the treatment of keloids, but because of its overt side effects we used 5-FU in combination with TAC for keloid treatment in our study. The rationale of our study is to provide efficacious and dependable treatment option for this cosmetically disfiguring and therapeutically challenging dermatological problem. The results of this study will give a recommendation towards the better treatment of keloids.

Methods

This Randomized Controlled trial was conducted in the Department of Dermatology, DHQ Hospital, Faisalabad, during the period of one year, from February 2018 to February 2019. Patients were included in the study via Non-probability consecutive sampling. 150 clinically diagnosed patients with keloids of either sex, age ranging from 20 to 50 years, presenting with pain, tenderness, pruritus, restriction of movement and cosmetic disfigurement (patients having 2 or more of these signs/ symptoms) were included in the study after taking written informed consent. Patients taking any treatment in the past 6 months, patients with chronic renal failure, pregnant and lactating females were excluded from the study.

Detailed history and clinical examination was done. Photographs were taken before the start of

therapy and size of keloid was measured by dialed caliper. Patients with keloid were randomly divided in two equal groups by computer generated random number table. Local anesthesia was given in the form of injection xylocaine sublesionally in both groups. In group A injection 5-FU 10mg/ml (0.2ml) plus triamcinolone acetonide 10mg/ml (0.25ml) was given intralesionally 2mm apart. In group B injection triamcinolone acetonide 10mg/ml (0.25ml) alone was given 2mm apart. Dose was repeated after 3 weeks in each group for a total duration of 3 months. Photographs were taken at the end of 14 weeks and size was also measured. Monitoring was done by assessing the reduction in size of keloid (length, width & breadth) in terms of percentage by caliper. Efficacy was measured in terms of >75% reduction in size of keloids (measured by a dialed caliper) from baseline till the end of 14 weeks.

All the data was analyzed by using SPSS-10. Mean and standard deviation were calculated for all quantitative variables like age and size of keloid at baseline, and at 14 weeks in both groups. Frequency and percentages were calculated for all qualitative variables like gender and excellent response in both groups. Chi-square test was used to compare excellent response between two groups. P-value<0.05 was taken as significant.

Results

A total of 150 cases, 75 in each group, were studied. Patients ranged between 20-50 years of age. Mean age was 25.78±8.54 and 26.09±8.21 years in group-A and group-B respectively. Age distribution of patients is shown in **Figure 1.**

There were 37 males (49.33%) in group-A and 42 males (56%) in group-B while 38 females (50.67%) in group-A and 33 females (44%) in group-B **(Figure 2)**.

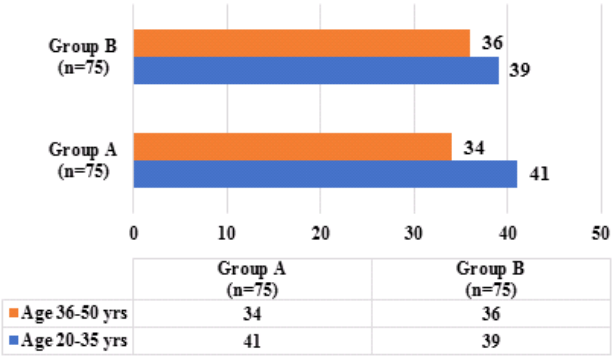

Figure 1 Age Distribution (n=150).

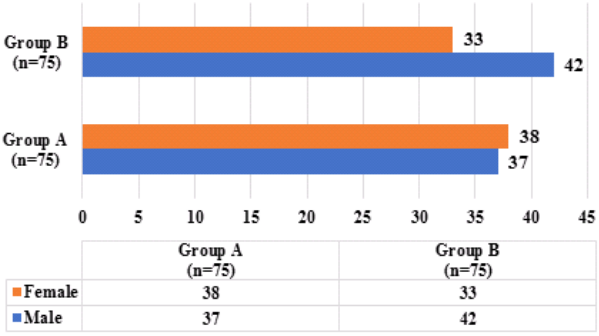

Figure 2 Gender Distribution (n=150).

Table 1 Mean size of Keloids (n=150).

Mean size of Keloids (mm)	*Group A (n=75)* *No.*	*Group B (n=75)* *No.*
At Baseline	7.84 ± 3.50	8.48 ± 3.08
At 14th Week	3.10 ± 2.79	4.36 ± 2.81

Table 2 Comparison of efficacy of intralesional 5 FU plus TAC vs intralesional TAC alone (n=150).

Efficacy	*Group A (n=75)* *No. (%)*	*Group B (n=75)* *No. (%)*
Yes	43 (57.33%)	27 (36%)
No	32 (42.67%)	48 (64%)
Total	75 (100%)	75 (100%)

Mean size of the keloids at baseline was recorded as 7.84±3.50 mm in Group-A and 8.48±3.08 mm in Group-B. Whereas, mean size of the keloids at 14th day was recorded as 3.10±2.79 mm in Group-A and 4.36±2.81 mm in Group-B **(Table 1)**.

Comparison of efficacy of intralesional 5-FU plus steroid vs intralesional steroid alone in the treatment of keloid revealed that 57.33% (n=43) in Group-A and 36% (n=27) in Group-B achieved efficacy **(Table 2).** The difference in

Table 3 Stratification by Age (n=70).

Age (Years)	*Group A (n=43)* No. (%)	*Group B (n=27)* No. (%)
20-35	24 (55.81)	17 (62.96)
36-50	19 (44.19)	10 (37.04)
Total	43 (100)	27 (100)

Table 4 Stratification by Gender (n=70).

Gender	*Group A (n=43)* No. (%)	*Group B (n=27)* No. (%)
Male	22 (51.16)	15 (55.56)
Female	21 (48.84)	12 (44.44)
Total	43 (100)	27 (100)

efficacy in both groups was statistically significant (p value 0.00).

Stratification for age was done which showed that out of 43 patients achieving efficacy in Group-A 55.81% (n=24) were between 20-35 years and 44.19% (n=19) were between 36-50 years of age. Whereas, in Group-B out of 27 patients achieving efficacy, 62.96% (n=17) were between 20-35 years and 37.04% (n=10) were between 36-50 years of age **(Table 3)**.

Stratification for gender was done which revealed that out of 43 patients achieving efficacy in Group-A 51.16% (n=22) were males and 48.84% (n=21) were females. Whereas, in Group-B out of 27 patients who achieved efficacy, 55.56% (n=15) were males and 44.44% (n=12) were females **(Table 4)**.

Discussion

Keloid, an abnormal disfiguring scar, is benign hyperproliferative growth of dermal fibroblasts that extends beyond the margin of original wounds. It does not regress spontaneously and has a tendency to recur after excision. Keloid becomes raised within 3-4 weeks of the triggering stimulus.[9] Keloid is a cause of considerable cosmetic concern and poses a therapeutic challenge to the dermatologists due to its tendency to recur despite appropriate treatment.

Intralesional triamcinolone has traditionally been the mainstay of treatment and in conjunction with excision has yielded efficacy rates between 58% and 93%.[10] Intralesional TAC causes inhibition of protein synthesis and fibroblast migration.[9] There are many reports of treatment failures associated with the use of intralesional steroids. Also, adverse effects including hypopigmentation, atrophy, and telangiectasias limits its use.[8] Intralesional 5-FU has antimetabolic activity and inhibits fibroblasts proliferation.[11] The immediate side effects associated with injection 5-FU are pain, stinging sensation, purpura at injection site and occasionally superficial ulceration.[12]

Multiple therapeutic modalities have been tried previously to find an effective treatment option for keloids but none has shown consistent results. The present study has been conducted to compare the efficacy of intralesional 5-FU plus TAC versus intralesional TAC alone in the treatment of keloids. With this study we intended to provide a better treatment option for keloids and local evidence of the efficacy of the suggested treatment modality.

In our study, efficacy in group A (intralesional 5-FU plus TAC) was achieved in 43 (57.33%) patients while in group B (intralesional TAC alone) 27 (36%) of patients showed efficacious results. The difference between the efficacy in both groups was found to be statistically significant (p value – 0.00).

The results of our study are also consistent with another study done by Khan *et al*.[4] in which the combination of 5-FU and TAC (84% of patients achieving efficacy) was found to be superior as compared to TAC alone (68% of patients achieving efficacy).[4]

The findings of our study are consistent with a study done by Sharma *et al*.[9] which also showed

better results in case of combination therapy i.e. injection 5-FU plus TAC (52% patients achieving excellent response) as compared to 5-FU alone where efficacy was achieved in only 32% of patients.[9]

Another study by Wu *et al.*[13] showed an efficacy of 97.14%. The results of our study are comparable with those reported in the study conducted by Davison *et al.*[14] where average size reduction was 84%. However, our results are different from the studies conducted by Asilian *et al.*[8] and Darougheh *et al.*[15] where duration of treatment was less than 10 weeks.

The results in this study suggest that combination of 5-FU plus TAC is superior in efficacy compared to intralesional steroid alone therapy. The success of 5-FU in those particularly intractable keloid cases where steroids have failed is significant. Long-term prospective trials using anti-neoplastic agents are needed to properly establish an ideal treatment regimen for this challenging problem.

Conclusion

We conclud that the efficacy of intralesional 5-Flurouracil plus triamcinolone acetonide is significantly higher than intralesional triamcinolone acetonide alone for the management of keloid.

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