ORIGINAL ARTICLE

Comparison between the Efficacy of Intra-Lesional Triamcenolone and Combination of Triamcinolone With 5-Fluorouracil in the Treatment of Keloid and Hypertrophic Scars

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ABSTRACT

Aim: To compare the efficacy of intra-lesionaltriamcenolone combined with 5-fluorouracil versus triamcenolone alone in the treatment of keloids and hypertrophic scars

Methods: This randomized controlled trial was conducted at Department of Plastic Surgery& Burn Unit, Sheikh Zaid Hospital Rahim Yar Khan from May 2015 to November 2015. Total 62 patients with keloid or hypertrophic scar measuring >1 cm in size, either male or female having age 15-60 years were selected for the study.

Results: The mean age of patients in group A was 31.71±8.13years and in group B was 32.01±7.87years. Out of 62 patients, 61.29% were females and 38.71% were males with male to female ratio of 1.58:1. Efficacy of Group A (intra-lesionaltriamcenolone combined with 5-fluorouracil) was 64.52% while in Group B (intra-lesionaltriamcenolone alone) was 29.03% with p-value = 0.005 which is statistically significant.

Conclusion: This studyconcluded that intra-lesionaltriamcenolone combined with 5-fluorouracil is better and more efficacious than intra-lesionaltriamcenolone alone in the treatment of keloids and hypertrophic scars.

Keywords: Corticosteroid, 5-fluorouracil, combination therapy, reduction in size, skin atrophy.

INTRODUCTION

Keloids also called benign fibro-proliferative scars as it grows beyond the confines of original wound and invades surrounding skin. Keloids does not regress and tends to reoccur after excision[1]. On the other hand, hypertrophic scars are erythematous raised lesions that does not expand beyond the boundaries of injury and it may regress spontaneously[2].

The incidence of keloids formation ranges from 4.5% to 16% more commonly in darker-skinned people[3]. Many factors like genetic and environmental seems to be involved in keloids formation but exact etiology is not known. Main cause of development of keloids and hypertrophic scars is trauma to skin which may be physical and pathological[4,5].

There is no universally accepted treatment resulting in permanent ablation of these scars[6]. The high recurrence rate has initiated a wide variety of treatments, such as, compression therapy, intralesional injections of corticosteroid, 5-fluorouracil, methotrexate, bleomycin, radiotherapy, cryosurgery, laser therapy, tamoxifen, and tacrolimus[7,8].

Due to unsatisfactory results with individual therapy of the above mentioned modalities, combination of two therapies have been used and found to be more effective. Intra-lesional steroid injections have been the mainstay of keloid & hypertrophic scars treatment for a long time due to its tolerability and effectiveness in reducing the symptoms[7]. Intra-lesional steroid used in combination with 5-Fluorouracil has also found a place in the treatment of keloids and hypertrophic scars and is found to be more acceptable to patients due to the faster results achieved in comparison to intralesional steroid alone[9].

The rationale of this study was to compare the efficacy of intra-lesional triamcenolone combined with 5-fluorouracil versus triamcenolone alone in the treatment of keloids and hypertrophic scars in local population. As intra-lesional triamcenolone alone is routinely used for these particular patients so, the results of this study would help us to evaluate its efficacy when used in combination with 5-fluorouracil and made some practical recommendations in our routine practice guidelines for treating the keloids and hypertrophic scars.

MATERIAL AND METHODS

This randomized controlled trial was conducted at Department of Plastic Surgery& Burn Unit, Sheikh Zaid Hospital Rahim Yar Khan from May 2015 to November 2015. Total 62 patients with keloid or hypertrophic scar measuring >1 cm in size, either

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male or female having age 15-60 years were selected for the study.

Patients with chronic renal or liver diseases, patient taking treatment for the keloids from last 3 months and pregnant/lactating women or those planning for pregnancy were excluded from the study.

Keloid is defined as: overgrowth of dense fibrous tissue that was usually developed after healing of a skin injury and was extended beyond the borders of the original wound was deemed as positive.

Hypertrophic scars are defined as: erythematous, pruritic, raised fibrous lesions that typically was not expanded beyond the boundaries of the initial injury was deemed as positive. Permission was taken from the institutional review committee before commencing the study.All the selected patients were randomly divided into two groups i.e., Group A and Group B.

Group A patients were given intra-lesionaltriamcenolone combined with 5-fluorouracil while Group B patients were given intra-lesional triamcenolone alone. In all patients, injection was given by the same Plastic Surgeon.

Group A were treated once weekly with intralesional injection of triamcenolone 4 mg (0.1 ml of 40 mg/ml TAC) mixed with 5-fluorouracil 45 mg (0.9 ml of 50 mg/ml 5-FU) for a total of 8 sessions. Group B were treated with once weekly intralesional TAC 10mg (0.25ml of 40mg/ml TAC diluted with 0.75ml injectable normal saline) for a total of 8 sessions. In all patients, the solution was injected in the body of scar by using a 1cc syringe with premounted 27G needle by one surgeon. All patients were followed till 4 weeks after end of treatment and efficacy was noted as follows: Efficacy was deemed as yes if there was more than 50% reduction in initial keloid or hypertrophic scars in terms of observer scar assessment (by measuring size of the scar measured by a scale) and absence of all complications i.e., skin atrophy (thinning of the skin over the scar area), hypopigmentation (lightening of skin complexion), telangiectasias (dilated superficial blood vessels) and skin ulceration (discontinuity of the skin), 4 weeks after the end of treatment. Efficacy was deemed as no if there was < 50% reduction in initial keloid or hypertrophic scars in terms of observer scar assessment (by measuring size of the scar measured by a scale) or presence of any of the following complications i.e. skin atrophy (thinning of the skin over the scar area), hypopigmentation (lightening of skin complexion), telangiectasias (dilated superficial blood vessels) and skin ulceration (discontinuity of the skin), 4 weeks after the end of treatment. All the data was entered on pre-designed proforma along with demographic profile of the patients.

Statistical analysis was performed using SPSS version 16. Results were presented as mean and standard deviation for quantitative variables. Frequency and percentage was calculated for qualitative variables. P value ≤0.05 was considered as significant.

RESULTS

Age range in this study was from 15-60 years with mean age of 31.76±8.09 years. The mean age of patients in group A was 31.71±8.13 years and in group B was 32.01±7.87 years. Efficacy (> 50% reduction in initial keloid or hypertrophic scars and absence of all complications after the end of 4 weeks treatment) of Group A (intra-lesionaltriamcenolone combined with 5-fluorouracil) was 20(64.52%) while in Group B (intra-lesionaltriamcenolone alone) was 09 (29.03%) as shown in Table I1 (p-value=0.005). Comparison between efficacy of both groups according to age groups has shown in Table 2 which showed significant difference of efficacy between both groups among 15-30 years of age. Table 3 has shown comparison between efficacy of both groups according to gender and significant difference was found among female patients but no significant difference among male patients. Stratification of type of scar with respect to efficacy has shown in Table 4.

Table 1: Comparison of efficacy between both Groups.

Study group	Efficacy		Total
	Yes	No	
A	20(64.52%)	11(35.48%)	31
B	9(29.03%)	22(70.97%)	31

P value is 0.005 which is statistically significant

Table 2: Comparison between efficacy of both groups according to age.

Age	Group A (n=31)		Group B (n=31)		P-value
	Efficacy		Efficacy		
	Yes	No	Yes	No	
15-30	11 (68.75%)	05 (31.25%)	05 (33.33%)	10 (66.67%)	0.049
31-45	06 (60.0%)	04 (40.0%)	03 (30.0%)	07 (70.0%)	0.178
46-60	03 (60.0%)	02 (40.0%)	01 (20.0%)	05 (80.0%)	0.137

Table 3: Comparison between Efficacy of both groups according to Gender.

Gender	Group A (n=31)		Group B (n=31)		P-value
	Efficacy		Efficacy		
	Yes	No	Yes	No	
Male	11 (61.11%)	07 (38.89%)	06 (30.0%)	14 (70.0%)	0.054
Female	09 (69.23%)	04 (30.77%)	03 (27.27%)	08 (72.73%)	0.041

Table 4: Comparison between Efficacy of both groups according to Type of Scar.

Type of Scar	Group A (n=31)		Group B (n=31)		P-value
	Efficacy		Efficacy		
	Yes	No	Yes	No	
Keloid	12 (66.67%)	06 (33.33%)	04 (21.05%)	15 (78.95%)	0.005
Hyperterophic Scar	10 (66.67%)	05 (33.33%)	05 (35.71%)	09 (64.29%)	0.096

DISCUSSION

Main treatment of keloids is pharmacological therapy in combination of other therapies[10]. Out of pharmacological therapies steroid injection is most commonly used as intralesional injections. Injection triamcinolone is used intralesionally both for hypertrophic scar and keloids causing flattening, fading and decrease in symptoms like itching. The dose of injection can vary from 10 to 120 mg depending on size of scars[11].

In our study, the mean age of patients in group A was 31.71±8.13years and in group B was 32.01±7.87years with majority of the patients 31 (52.0%) were between 15 to 30 years of age. Onset occurs most commonly in individuals aged 10-30 years. Keloids occur less frequently at the extremes of age.[12] Also in our study, out of 62 patients, 38 (61.29%) were females and 24 (38.71%) were males with male to female ratio of 1.58:1. Similar findings were also observed in many previous studies that scars occur commonly between 2nd and 3rd decade of life with male predominance[3,6,7].

In our study, Efficacy (>50% reduction in initial keloid or hypertrophic scars and absence of all complications after the end of 4 weeks treatment) of Group A (intra-lesionaltriamcenolone combined with 5-fluorouracil) was 20 (64.52%) while in Group B (intra-lesionaltriamcenolone alone) was 9(29.03%) (p-value= 0.005). A study shown better efficacy of intra-lesionaltriamcenolone combined with 5-fluorouracil compared to triamcenolone alone (55% versus 20%) in terms of reduction in size and complications rate[8].

Many previous studies have also shown that combination 5-FU/triamcinolone may be superior in efficacy compared to intralesional steroid therapy.[13-14]In one study, the most effective regimen was found intra-lesionaltriamcenolone combined with 5-fluorouracil.[3] A total of 85% of keloids showed more than 50% improvement in an open study by Kontochristopoulos et al[15].

Davison SP et al[3] in a retrospective review of 102 keloids concluded that combination 5-FU/triamcinolone is superior to intralesional steroid therapy in the treatment of keloids.

Prabhu A et al[7] in their randomized study of 5-FU versus triamcinolone acetonide reported significantly better reduction in the size of the keloid in 5-FU group (71.23%) than in triamcenoloneacetonide (57.48%) with a *P* value of 0.04.

Darzi MA observed that intralesional triamcinolone acetonide produced symptomatic relief in 72% and complete flattening in 64% of the lesions.[16] However, Kill J noticed complete flattening of the lesions and cessation of itching in 52 (100%) of the cases.[17] The study conducted by Nanda S observed more than 50% improvement in the size in almost 80% of cases that were been treated with 5-flurouracil.[18]Kontochristopoulos G et al[6] reported morethan 50% improvement in size in 85% of the patients,

Sharma S et al[9] in his study reported good to excellent results in 96% patients with this combination and also more acceptable to patients. The efficacy in terms of patient and observer assessment in TAC group patients is 20% and 15% respectively as compared to 55% and 40% in TAC + 5-FU in a study (in both keloids and hypertrophic scars).[19]

So, on the whole it is concluded intra-lesionaltriamcenolone combined with 5-fluorouracil is an effective way to treat keloids and hypertrophic scars. It may be better option than the intra-lesionaltriamcenolone alone and should be used routinely in our general practice in order to reduce the morbidity.

CONCLUSION

This studyconcluded that intra-lesionaltriamcenolone combined with 5-fluorouracil is better and more efficacious than intra-lesionaltriamcenolone alone in the treatment of keloids and hypertrophic scars. So,

we recommend that intra-lesionaltriamcenolone combined with 5-fluorouracil should be used routinely in these particular patients instead of intra-lesionaltriamcenolone alone in order to reduce the size of keloid or hypertrophic scars and without any complication which will ultimately reduce their morbidity.

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