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Original Research Paper

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COMPARATIVE STUDY OF EFFICACY AND SAFETY OF INTRALESIONAL TRIAMCINOLONE ACETONIDE VERSUS INTRALESIONAL 5-FLUOROURACIL VERSUS COMBINATION OF BOTH IN MANAGEMENT OF KELOIDS

Dr. Himani Tandon Junior Resident, Department Of Dermatology, Venereology And Leprosy, Rohilkhand Medical College And Hospital, Bareilly, Uttar Pradesh.

Dr. Anuj Kumar* MD, Senior Resident, Department Of Dermatology, Teerthanker Medical College And Hospital, Moradabad, Uttar Pradesh. *Corresponding Author

Dr. P. K. Rathore MD, Professor And Head Of Department, Department Of Dermatology, Venereology And Leprosy, Rohilkhand Medical College And Hospital, Bareilly, Uttar Pradesh.

ABSTRACT

BACKGROUND: keloid is a benign overgrowth of fibrotic tissue and are aesthetically unacceptable to the patients. Management is difficult and pose a challenge for physicians. This study compares the efficacy and safety of intralesional triamcinolone acetonide, intralesional 5-fluorouracil and combination of both in management of keloids.

METHOD: Total 60 patients, randomly divided into three groups: A, B, C were subjected to intralesional Triamcinolone acetonide, 5- Fluorouracil and their combination respectively, every 3weeks for 18 weeks and assessed with Vancouver Scoring Scale.

RESULTS: Improvement seen in all parameters, maximum with combination of triamcinolone and 5-fluorouracil.
Major side effects were hypopigmentation with intralesional triamcinolone; pain and hyperpigmentation with intralesional 5-fluorouracil and mild pain with combination of two.

CONCLUSION: Combination of 5-fluorouracil and triamcinolone acetonide seemed to be more effective with lesser side effects than the other two.

KEYWORDS : Keloid, Triamcinolone Acetonide, 5-fluorouracil

INTRODUCTION

Keloids are elevated fibrous scars occurring after an injury heals, extending beyond the original wound and do not regress.[1] They lead to aesthetic and physical complaints with functional impairment, causing psychogenic turmoil and depression in affected individual. Hypertrophic scar is similar to keloid except it remains confined to the original defect and tends to resolve within few months.

Keloid management has been a constant disappointment. Various treatment options are available such as intralesional corticosteroids, 5-fluorouracil, compression therapy, cryosurgery, etc., but no single modality has been proved to be very effective.[2] Triamcinolone acetonide (TAC) is a potent and most commonly used corticosteroid. It suppresses inflammation, inhibits fibroblast proliferation and collagen synthesis.[3] However, there is a risk of telangiectasia, atrophy and pigmentary change. 5-flurouracil (5FU) is a pyrimidine analogue, with antimetabolite activity, which inhibits synthesis of deoxyribonucleic acids. The rapidly proliferating fibroblasts are halted and scar degradation is promoted. But it may cause potentially serious local side effects such as pain, hyperpigmentation, ulceration and burning sensation.[4] Combining both triamcinolone acetonide and 5-fluorouracil has shown to provide faster and better results with lesser side effects.

This study was done to compare the efficacy and adverse effects of Intralesional triamcinolone acetonide, Intralesional 5-Flurouracil and the combination of both in treatment of Keloids.

MATERIALS AND METHODS

The study was done in Outpatient Department of Dermatology, Venereology and Leprosy, RMCH, Bareilly, Uttar Pradesh from November 2017 till October 2018. The study protocol was approved by the institutional ethics committee. Also, an informed consent was obtained from patient/guardian.

INCLUSION CRITERIA:

Those willing for the study and regular follow up, aged between 11 to 60 years. Patients willing not to undertake any other keloid treatment, keep the keloid and surrounding area clean and report immediately if any side effects appeared.

EXCLUSION CRITERIA:

Patients on treatment with oral isotretinoin within past 6 months, immunocompromised, pregnant and lactating mothers and those who had local infection at the site of keloid.
A total of 60 patients randomly allocated into three groups: A, B and C were treated with intralesional triamcinolone acetonide (20mg/ml), intralesional 5-fluorouracil (50mg/ml) and combination of both, 0.9 ml 5-fluorouracil (50mg/ml) and 0.1ml triamcinolone (40mg/ml) respectively, every 3weeks for 18 weeks. Relevant history and proper examination were done before the first session. Height, vascularity, pigmentation and pliability of keloid was assessed on Vancouver score scale. Outcome was judged by the investigator using Vancouver score scale (VSS) and patient according to visual analogue scale (VAS).

INJECTION TECHNIQUE:

Triamcinolone acetonide injection (40mg/ml) was diluted with lignocaine in 1:1 ratio to obtain desired concentration of 20mg/ml. 5-fluorouracil injection is available in the desired concentration of 50mg/ml. The combination was prepared with 0.9ml of 50mgl/ml 5-fluorouracil and 0.1ml of 40mg/ml of triamcinolone acetonide. The drug was injected within the lesion thoroughly until uniform and complete blanching using a disposable tuberculin syringe with 26-gauze needle.

THE VANCOUVER SCORING SCALE[5]:

I. VASCULARITY

0	–	Normal
1	–	Pink
2	–	Red
3	–	Purple

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II. PIGMENTATION

0	–	Normal
1	–	Hypopigmentation
2	–	Hyperpigmentation

III. HEIGHT

0	–	Normal-flat,
1	–	<2mm,
2	–	2-5mm,
3	–	>5mm

IV. PLIABILITY

0	–	normal
1	–	supple
2	–	yielding
3	–	firm
4	–	banding
5	–	contracture

VISUAL ANALOGUE SCALE (VAS)[6]:

for assessment of response by patient.

between 7 to 10	-	"excellent" response
between 4 to 7	-	"good" response
below 4	-	"poor" response.

STATISTICAL TOOLS EMPLOYED:

Data entered on Microsoft Excel spreadsheet was imported into SPSS version 22 for statistical analysis. Data presented in mean and standard deviation. One-way Anova used to find significant difference between different variables in different groups and independent Chi-square test was performed to find association. A *P*-value <0.05 was considered statistically significant.

OBSERVATIONS & RESULTS

The study was done on 60 patients, meeting all the inclusion and exclusion criteria, aged 11years to 60years, after obtaining an informed and written consent. The baseline characteristics were comparable in all three groups (Table 1).

TABLE 1: BASELINE CHARACTERISTICS OF PATIENTS

Variable	GROUP A (TAC)	GROUP B (5FU)	GROUP C (TAC+5FU)	p-value
Number of patients	20 (33.33%)	20 (33.33%)	20 (33.33%)	
Age (mean +/- SD) (years)	27.85 ± 12.81	29.7 ± 12.11	31.3 ± 13.89	0.702
Gender, No. (%)				
Male	15 (75%)	14 (70%)	10 (50%)	0.99
Female	5 (25%)	6 (30%)	10 (50%)	
Mean duration of keloids	34.9 ± 40.14	19.65 ± 23.52	26.85 ± 43.22	0.426
Mean number of keloids	2.05 ± 1.67	1.7 ± 1.03	1.55 ± 1.14	0.47
Positive family history	9 (45%)	6 (30%)	6 (30%)	0.99
Positive H/O prior trauma	14 (70%)	15 (75%)	13 (65%)	0.99

The most common site of keloid development was chest followed by shoulder and back (Table 2)

TABLE 2: SITE OF KELOID DEVELOPMENT

SITE	GROUP A (TAC)	GROUP B (5FU)	GROUP C (TAC+5FU)
	NO. (%)	NO. (%)	NO. (%)
Arm	2 (10%)	3 (15%)	1 (5%)
Back	2 (10%)	2 (10%)	3 (15%)
Chest	10 (50%)	10 (50%)	8 (40%)
Face	2 (10%)	1 (5%)	2 (10%)
Forearm	1 (5%)	1 (5%)	0
Leg	2 (10%)	1 (5%)	3 (15%)
Shoulder	1 (5%)	2 (10%)	3 (15%)

The most common complaint associated with keloid was itching, followed by pain. One patient also complaint of pricking sensation. (Table 3)

TABLE 3: ASSOCIATED COMPLAINTS

Associated Complaints	Group A (TAC)	Group B (5FU)	Group C (TAC+5FU)
	NO. (%)	NO. (%)	NO. (%)
Itching	10 (50%)	10 (50%)	5 (25%)
Pain	2 (10%)	5 (25%)	4 (20%)
Pricking sensation	0	1 (5%)	0

There was no significant difference in pre-treatment VSS scores in all three groups. VSS score was assessed at every sitting. Maximum improvement was seen with combination of both triamcinolone and 5-fluorouracil (Figure 1) followed by triamcinolone alone (Figure 2) and 5-fluorouracil alone (Figure 3). Difference in post-treatment VSS score and mean percentage improvement in three groups was statistically very significant (TABLE 4)

TABLE 4: VSS SCORE

VARIABLE	GROUP A (TAC)	GROUP B (5FU)	GROUP C (TAC+5FU)	P-VALUE
Mean pre-treatment VSS	9.25 +/- 2.07	9.2 +/- 2.04	9.3 +/- 1.75	0.987
Mean post-treatment VSS	4.3 +/- 1.92	5.1 +/- 2.4	3.35 +/- 2.207	0.047
% improvement in VSS	55.6 +/-14.68	46.9 +/- 17.57	65.21 +/- 18.33	0.0049

*p-value <0.05: significant

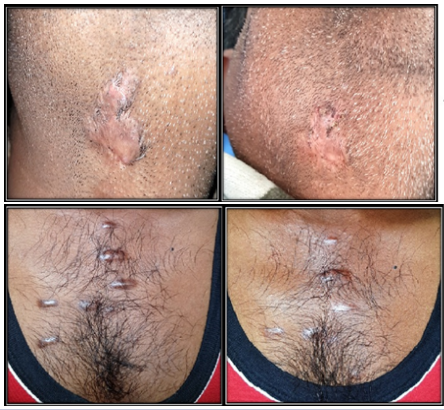

FIGURE 1

FIGURE 2

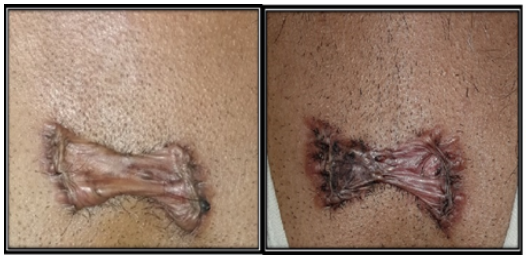

FIGURE 3

The most common adverse effect associated with intralesional triamcinolone was hypopigmentation. With intralesional 5-fluorouracil, was pain and hyperpigmentation. Although, ulceration was seen in two patients. Patients who received combination of both, complaint of mild pain only. (Table 5)

TABLE 5: ADVERSE EFFECTS

ADVERSE EFFECTS	GROUP A (TAC) N0. (%)	GROUP B (5FU) N0. (%)	GROUP C (TAC+5FU) NO. (%)
Pain	6 (30%)	19 (95%)	8 (40%)
Hypopigmentation	7 (35%)	0	0
Atrophy	1 (5%)	0	0
Telangiectasia	2 (10%)	0	0
Ulceration	0	2 (10%)	1 (5%)
Hyperpigmentation	0	10 (50%)	0

DISCUSSION:

Keloids, rightly called benign fibro-proliferative scars, are an abnormal proliferation of scar tissue formed at the site of trauma growing beyond the original boundaries of the lesion.
Treatment of keloids is very challenging and controversial. Pharmacological therapy is the mainstay as surgical excision causes almost 100% relapse. Various modalities have been tried with an acceptable response. Out of these, corticosteroid injections are the most accepted due to easy availability, low cost and less side-effects with a lower dose. They reduce glycosaminoglycans and collagen synthesis, inhibits fibroblasts growth and promote collagen and fibroblasts degradation, causing lesion to flatten along with relief in symptoms.[7] Side effects like telangiectasia, skin atrophy and hypopigmentation have been noted.

5-fluorouracil blocks the collagen synthesis by blocking thymidylate synthase, thus interfering with the synthesis of RNA. It also inhibits fibroblast proliferation, and collagen gene associated with TGF- expression. 5-fluorouracil is also easily available, very cost effective but associated with few potentially distressing local side effects like ulcerations and burning sensation.[4]

Combining triamcinolone acetonide with 5-fluorouracil counteracts the adverse effects of 5-Fluorouracil due to anti-inflammatory action of triamcinolone acetonide.

The study compares the efficacy and safety of Triamcinolone, 5-Fluorouracil and their combination in treatment of keloids, using the Vancouver Scar scale to assess improvement. All three study groups were statistically similar in terms of demographic variables, clinical picture and scar severity at baseline.

Majority patients showed significantly higher reduction in the mean VSS score with the combination of triamcinolone and 5-fluorouracil followed by triamcinolone alone and 5-flurouracil alone.

Pain at the site of the injection was the immediate side effect noticed in all three groups. It was bearable and transient. But it persisted in majority of patients treated with intralesional 5-fluorouracil. Although, the daily routine activities were not affected.

Hypopigmentation was a major drawback with triamcinolone acetonide injections. Majority patients treated with 5-fluorouracil complaint of pain and hyperpigmentation. Also, two patients complaint of ulceration following the injection. Only mild pain was observed with combination of triamcinolone acetonide and 5-fluorouracil.

CONCLUSION:

Better and faster response was seen with combination of triamcinolone acetonide and 5-fluorouracil. Also, side-effects were less frequent, milder and acceptable with the combination. Physician's assessment also showed the same results.

LIMITATIONS OF THE STUDY:

Amount of drug used with respect to the area and thickness of keloid could not be measured as the thickness varies from one lesion to another and within the same lesion also. Hence, complete blanching while injecting the drug was considered to be the end point.

The therapeutic response was studied only up to 22 weeks i.e 4 weeks after the last injection. Hence, nothing can be said about the recurrences.

CONFLICTS OF INTEREST

None

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