



A COMPARATIVE STUDY OF EFFICACY OF INTRALESIONAL TRIAMCINOLONE, INTRALESIONAL BLEOMYCIN AND INTRALESIONAL 5-FLUOROURACIL IN KELOID

Dermatology

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ABSTRACT

BACKGROUND- Despite many advances in the understanding of wound healing and scar formation, the treatment of keloid is still controversial. The aim of this study was to evaluate the efficacy and safety of intralesional triamcinolone, intralesional bleomycin and intralesional 5-fluorouracil in the treatment of keloid.

METHODS- Total 90 patients were randomly divided into three groups (group A, B, C). Group A patients were given intralesional triamcinolone (Regimen I) 40mg/ml, group B patients were given intralesional 5-fluorouracil (Regimen II) 50mg/ml and group C patients were given intralesional bleomycin (Regimen III) 1 IU/ml. The efficacy of different treatment modalities were analyzed by evaluation of response to treatment, side effects and recurrence during follow up period.

RESULTS- In regimen I, 20 (66.67%) patients showed excellent response and in regimen II, 13 (43.33%) patients showed excellent response. 12 (40%) out of 30 patients showed recurrence in regimen I, followed by 5(16.67%) in regimen II, and 8 (26.67%) in regimen III, Local pain after injection was noted to be maximum in 7 patients followed by 6 patients and 5 patients in regimen III, II and I respectively .

CONCLUSION- In terms of response to treatment, there was no significant difference found between response of regimen I Vs II and II Vs III. Regimen III was found less effective in comparison to regimen I which is statistically significant.

KEYWORDS

Keloid, Triamcinolone, 5-fluorouracil, Bleomycin

INTRODUCTION

Keloids are dermal fibroproliferative disorder unique to humans that occur following trauma, inflammation, surgery, and sometimes occur spontaneously¹. Keloid tissue extends beyond the borders of the original wound, does not regress spontaneously and tends to recur after excision².

Despite many advances in the understanding of wound healing and scar formation, the treatment of these conditions is still controversial¹. Although keloids occur with a considerable frequency, no single therapeutic modality has been determined experimentally to be very effective for treating them. Effective keloid management still remains a distant dream in spite of many recent modalities being tried for the same. Although many treatment protocols have shown efficacy of varying degrees, there are very few systematic randomized trials comparing them in a given community. Thus, controversy continues to exist regarding the treatment of keloids.

This study was conducted to compare the efficacy of intralesional triamcinolone, intralesional bleomycin and intralesional 5-fluorouracil in keloid.

MATERIALS AND METHODS

This randomized clinical trial is an open evaluation to compare the effect of three different regimens (intralesional triamcinolone acetamide, 5-fluorouracil and bleomycin) on healing of keloids in three groups comprising 30 patients each.

After written informed consent patients presented with keloid who fulfilled selection criteria were included for the study. Inclusion criteria for the study were patients from either sex presented between 10 and 50 years of age, size of keloid more than 1 c.m. to 10 c.m. and on any site of body, duration of keloid <5years. The exclusion criteria were pregnancy or lactation, patients with systemic illness like diabetes mellitus, cancer and cardiac disease, mental disease on the basis of history, physical examination and investigation like blood sugar level, and ECG, patients on isotretinoin and anabolic steroids.

Total 90 patients were randomly divided into three groups (group A,B,C). Group A patients were given intralesional triamcinolone (**Regimen I**) 40mg/ml administered at intervals of 2 weeks, maximum up to 10 sittings. Group B patients were given intralesional 5-fluorouracil (**Regimen II**) 50mg/ml until the blanching appears at

interval of 2 weeks, maximum upto 10 sittings. The delivered dose was adjusted according to the extent of the lesions but did not exceed 100 mg/session (2 ml). Group C patients were given intralesional bleomycin (**Regimen III**) 1 IU/ml administered at intervals of 2 weeks, maximum up to 10 sittings. The dose delivered was adjusted according to the extent of the lesions but did not exceed 2 IU/session (2 ml). The injections were given after giving local anaesthesia to alleviate pain.

Patients were followed up initially biweekly then monthly for one year. Every time, lesions were examined regarding their pain, edema, bullae formation, ulceration, secondary infection, pigmentary changes, flatness and recurrence. Before and after photographs of lesions was taken for each patient after noting the dimensions of every lesion with the help of a scale. At the end of study period, the response to treatment in terms of flattening of the lesions was categorized as excellent: 76-100% improvement; good: 51-75% improvement; fair: 26-50% improvement; and poor: <25% improvement.

The efficacy of different treatment modalities were analyzed by evaluation of response to treatment, side effects and recurrence.

Results were expressed as number and percentage for each category. Categorical data was analysed by chi-square test to correlate between the groups. P value of 0.05 or less was considered for statistically significant.

Results:

Ninety patients, 49(55.4%)females and 41(45.6%)males were included in study from outpatient dept of dermatology, Mathura Das Mathur Hospital, Jodhpur. All patients completed the study. The total age of patients ranged from 11 to 50 and majority of the patients were between 21-30 years of age group. About half of the patients 54.44% had keloid of < 1 year duration. Chest was the commonest site (36.67%) followed by ear lobe (31.11%). Itching was the commonest presenting symptom seen in 56.67% of the patients. Trauma was the commonest predisposing factor (35.56%), followed by ear piercing (21.21%) and infection (21.21%). Family history of keloid was positive in only 7.78% of the patients.

As the results of the study were evaluated in terms of response to treatment, side effects and recurrence. The table.1 shows the response of all 90 patients treated under three different regimens.

Table. 1 Treatment Outcome In All Regimens

Regimen	Response of Patient								Total	%	Chi-Square	P-Value	Interpretation
	ER (>75%)	%	GR (51-75%)	%	FR (26-50%)	%	PR (<25%)	%					
I	20	66.67	7	23.33	3	10.00	0	0	30	100	20.986	.002	Significant Difference
II	13	43.33	8	26.67	6	20.00	3	10	30	100			
III	5	16.67	7	23.33	12	40.00	6	20	30	100			
Total	38	42.22	22	24.44	21	23.33	9	10	90	100			
Comparison between Regimen I & II											5.552	.136	No Difference
Comparison between Regimen II & III											6.622	.085	No Difference
Comparison between Regimen I & III											20.400	.000	Difference

ER-Excellent response, GR-Good response, FR-Fair response, PR-Poor response

In regimen-I, 30 patients were treated with intralesional triamcinolone acetonide (40mg/ml). Out of 30 patients, 20(66.67%) patients showed excellent response. Good response was seen in 7 (23.33%) and fair response in 3 (10%) patients. Relief of symptoms were seen in all patients. Most patients had dramatic improvement of symptoms by 1st or 2nd visit of treatment.



Figure.1 Regimen I : Intralesional triamcinolone acetonide before treatment



Figure.2: Regimen I: Intralesional triamcinolone acetonide after treatment

In regimen-II, 30 patients were treated with intralesional 5-fluorouracil (50mg/ml). Out of 30 patients, excellent response was seen only in 13 (43.33%) patients, 8 (26.67%) patients showed good response, followed by fair response in 6 (20%) and poor response in 3 (10%) patients. The symptoms of pain, pruritis responded to treatment in all 30 (100%) patients.



Figure.3: Regimen II : Intralesional 5-fluorouracil before treatment



Figure.4: Regimen II : Intralesional 5-fluorouracil after treatment

In regimen III, all patients were treated with intralesional bleomycin. Out of 30 patients, excellent response was seen only in 5 (16.67%) patients, 7 (23.33%) patients showed good response, followed by fair response in 12 (40%) and poor response in 6 (20%) patients.



Figure.5-Regimen III : Intralesional bleomycin before treatment



Figure.6: Regimen III: Intralesional bleomycin after treatment

Overall out of 90, 38(42.22%) patients showed excellent response (ER), 22(24.44%) showed good response (GR), 21(23.33%) fair response (FR) and least number of 9(10%) patients showed poor response (PR).

In terms of response to treatment, there was no significant difference found between response of regimen I Vs II and II Vs III. Regimen III was found less effective in comparison to regimen I which is statistically significant. Regimen I showed best results, with 20 (66.67%) patients showing excellent response followed by regimen II, in which 13 (43.33%) patients showed excellent response.

Out of 90 patients 40(44.44%) patients did not have any side effects. In regimen I, out of 30 patients, 5 (16.67%) patients developed atrophy, 2 (6.67%) patients had hypopigmentation, 1(3.33%) patient had depigmentation, 3(10%) patients had hypopigmentation + atrophy, 2(13.33%) patients had hypopigmentation + telengectasia and 4(13.33%) patient had pain. In regimen II, out of 30 patients, 6 (20%) patients had pain at injection site, 1 (3.33%) patient had pain + hyperpigmentation at injection site, 1 (3.33%) had pain + hyperpigmentation + ulcer, 2 (6.67%) patients had hypopigmentation + atrophy, 1 (3.33%) patient had hypopigmentation, 1(3.33%) patient had hyperpigmentation, 1 (3.33%) patient had Erythema+ Erosion, 1 (3.33%) patient had atrophy. In regimen III, out of 30 patients, 7 (23.33%) patients had local pain during injection and/or shortly after treatment, 2 (6.67%) patients had hyperpigmentation, 3(10%) patients had pain + hyperpigmentation + ulcer, 1 (3.33%) patient had hyperpigmentation + pain, 4 (13.33%) patients had erythema+erosion and 1(3.33%) patient had hypopigmentation + atrophy

The incidence of recurrence during the follow up period after the completion of treatment was seen maximum in 12(40%) out of 30 patients in regimen I, minimum in 5 patients(16.67%) in regimen II, and in 8 patients (26.67%) in regimen III. Difference in proportion of recurrence in different regimens was significant (p<0.05).

DISCUSSION

RESPONSE OF PATIENTS TO RESPECTIVE REGIMENS:

Various treatment modalities are available for keloids still lacking an effective one. A combination approach to therapy seems to be the best

option. So in this study, we compare three different treatment regimens. In this study, the primary outcome evaluated was the percentage of flattening as well regression in size of keloid, as a main parameter of efficacy. The three treatment regimens were comparable with respect to age, sex, site and duration of lesion, with statistically no significant difference ($p > 0.05$).

Regimen I: Intralesional triamcinolone

As the intralesional injection of corticosteroid (Triamcinolone acetonide) has always been the first line treatment for keloids. In our study, out of 30 patients 20 (66.67%) patients showed excellent response followed by good response in 7 (23.33%) patients and fair response in 3 (10%) patients. Relief of symptoms were seen in all patients. **Brain et al**¹ found significant response rate in 50-100% of cases. In the study of **Griffith**², 37 patients showed complete flattening of lesions in 19 (51%) patients and partial dissolution (softening) in 15 (40%) patients. In another study of **Griffith et al**³, out of 61 patients, 42 (69%) patients showed complete flattening (excellent response) of lesions and in 13 (21%) patients lesion became softer. Dramatic relief of symptoms was seen in all patients.

Regimen II: Intralesional 5-fluorouracil

Excellent and good response seen in 43.33% and 26.67% patients respectively which was higher than the study done by **Nanda et al**⁴ and **Gupta et al**⁵. **Kontochristopoulos et al**⁶ found that out of 20 patients, 17 (85%) patients showed more than 50% improvement.

Regimen III: Intralesional bleomycin

Response to bleomycin in form of excellent, good, fair, poor was lower than above two regimens. Bleomycin in the dose of 1.5 IU/ml injected intralesionally through multiple pricks resulted in flattening of lesions in 6 out of 13 cases in a study by **Espana A et al**⁷ similar to the study of **Badokh and Brun**⁸.

Side effects:

Maximum number of side effects were seen in regimen III, least were in regimen II followed by regimen I. In a study by **Manuskiatti and Fitzpatrick**, adverse effects like hypo or depigmentation, telangiectasia and atrophy are seen in about 20% of cases. Atrophy is less in regimen II and III. Side effects in all three regimens are comparable. **Griffith et al**³ in his study reported that use of intralesional Triamcinolone acetonide for treatment of keloid was associated with atrophy in 10 (16.4%) out of 61 patients and peripheral depigmentation in 2 (3.2%) patients. The side effects of triamcinolone acetonide were comparable with **Griffith**² study.

In regimen II, out of 30 patients 6 (20%) patients had pain at injection site, 1 (3.33%) patients had pain + hyperpigmentation at injection site and 1 (3.33%) had pain + hyperpigmentation + ulcer, 2 (6.67 %). **Gupta et al**⁵ reported that use of intralesional 5-fluorouracil has resulted mild to moderate hyperpigmentation at the site of injection in all patients, which gradually diminished after discontinuation of therapy. All patients experienced moderate to severe pain at the injection site and one patient developed an ulcer at the site of keloid.

In regimen III, out of 30 patients 7 (23.33%) patients had local pain during injection and or shortly after treatment and 2 (6.67%) patient had hyperpigmentation, 3 (10%) pain + hyperpigmentation + ulcer, 4 (13.33%) patients had Erythema+ Erosion.

Recurrence:

Maximum recurrence was seen in in regimen I (40%), followed by (16.67%) in regimen II, and (26.67%) of patients out of 30 in regimen III. Use of intralesional triamcinolone acetonide was associated with recurrence rate of 9-50% in a study by **Brain et al**¹ and 18% in a study **Griffith et al**³. **Kontochristopoulos et al**⁶ found that the use of intralesional 5-fluorouracil for treatment of keloid was associated with recurrence in 9 (47%) patients out of 19 patients. Recurrence in regimen II is less in compare to regimen I which is statically significant ($p < .045$).

Conclusion:

Thus in conclusion for the treatment of keloid intralesional 5-fluorouracil may be as effective as intralesional triamcinolone acetonide with lesser side effects and recurrence. However a larger study should be performed to confirm these findings.

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