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A PROSPECTIVE COMPARATIVE STUDY OF EFFICACY OF INTRALESIONAL TRIAMCINOLONE, INTRALESIONAL 5-FU AND COMBINATION OF TRIAMCINOLONE WITH 5-FU IN TREATMENT OF KELOIDS

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ABSTRACT

Aim: The aim of the present study was to compare the efficacy of intralesional triamcinolone, intralesional 5- FU and combination of triamcinolone with 5-FU in treatment of keloids.

Methods: The study was carried out on patients with keloid attending OPD of Department of Skin, V.D. and Leprosy, B. R. D. Medical College, Gorakhpur. Male and Female patients of 18 to 50 years of age with keloid to give consent for treatment were included. We took 60 patients for the study who were willing for the treatment after taking well informed consent from the patient.

Results: Male and female in group A and C are 50% each and in group B there are 70% males and 30% females. 47% of patients belonged to age group of 18- 30, 40% in age group of 31-40 and 13 % over 41 years. among study groups with 74% patients having keloid on chest and 16 % on back and 10% on arm. Among study groups where in traumatic etiology was more common with 70% of patients in group A, 50% patients in group B and 60% patients in group C followed by spontaneous and infective etiology. 2 patients from group B and group C having positive family history positive. Pigmentation grading according to vancouver scar scale with mean baseline value of group A, B and C as 1.60±0.55, 1.60±0.55 and 1.60±0.52 improving to 0.20±0.39, 1.2±0.31and 0.40±0.82 respectively after 24 weeks. In Group A telengiectasia, skin atrophy and hypopigmentation was seen whereas ulceration and pain was more common in Group B. There were no systemic side effects.

Conclusion: In our study the prevalence of keloids was found to be more in males than females. The majority of keloids were seen in the 18 to 40 years age group in our study. Etiology was divided into “infective,” “traumatic,” and, if there was no discernible etiology, “spontaneous. The maximum number (56%) of patients had traumatic etiology for development of keloids in our study. The other common etiology observed was spontaneous and infective in the descending order of frequency.

Keywords: Keloid; Triamcinolone; Fluorouracil, intralesional

1. INTRODUCTION

Keloids occur as a result of abnormal wound healing. The exact cause for this disorder remains elusive despite ongoing research standardized treatment and a high propensity for recurrence. This is evident in the wide range of available treatment modalities like surgical

ISSN: 0975-3583,0976-2833 VOL14, ISSUE6, 2023

excision, cryotherapy, laser therapy, low-dose radiation, silicone sheeting, topical retinoids and intralesional injections of steroid, 5-flurouracil (5FU) and bleomycin being employed.[1] All of these regimens are empirical, none of which guarantee a definite cure. Triamcinolone acetonide (TAC), a long-acting glucocorticoid has been the most popular drug and can presently be considered as gold standard in keloid treatment, alone or in combination.[1-3] A clinical efficacy ranging from 50-100% and a recurrence rate ranging between 9% and 50% has been reported., 5-flurouracil (5FU), a pyrimidine analogue, was first introduced in the treatment of keloid by Fitzpatrick who published his results in 1999.

Keloids are disorders of skin with unknown etiology where scar grows outside the original wound boundary. Healing of wounds is a complex physiologic response of the body to trauma and change in the arrangement of this process leads to scars that are exuberant.[5,6] They can be painful, itchy[7] and have an impact on the quality of life. Phenotypes vary due to differences of location, size and amount (raised, pigmented, painful, pruritic) of the lesion.[8,9] Approximately, 5-15% of the wounds can complicate into keloids and both sexes are equally affected although the incidence is higher amongst women. The average age of onset is 10-30 years. They may develop within a year of the injury and enlarge outside the boundary of the scar margin. High skin tension areas frequently develop keloids i.e. shoulders, chest, neck, flexor surface of extremities and wounds that cross the skin tension lines.

Secondary intention wound healing in which the healing time is above 3 weeks is considered as one of the important factors for keloid's development. Etiology of keloids is not clear, but is likely due to environmental and genetic factors. Keloids are scars that overgrow the original wound edges.[10,11] The cytokines transforming growth factor (TGF)-b has been implicated in the pathogenesis of keloid.[12,13] It is likely that the combination of raised levels of TGF-b and abnormal response of proliferative scar fibroblasts to this cytokineare important for keloid formation.[14]

The aim of the present study was to compare the efficacy of intralesional triamcinolone, intralesional 5- FU and combination of triamcinolone with 5-FU in treatment of keloids.

2. MATERIALS AND METHODS

The study was carried out on patients with keloid attending OPD of Department of Skin, V.D. and Leprosy, B. R. D. Medical College, Gorakhpur. Male and Female patients of 18 to 50 years of age with keloid to give consent for treatment were included. We took 60 patients for the study who were willing for the treatment after taking well informed consent from the patient.

Inclusion Criteria

- Male and Female from age 18 to age 50
- Keloids of size 1 to 10 cm in greatest dimension
- Keloids of >6 months duration.
- Patients who don’t have any history’ of bleeding disorder

Exclusion Criteria –

- Patient with hypertrophic scar
- Patients with bleeding disorder history
- Patient below the age of 18 and above age of 50
- Pregnant females
- Patients who had received treatment for keloids in the past 12 months,
- Those who had active inflammation,
- Infection or ulcer in or around the keloid,
- Immunosuppressed patients

ISSN: 0975-3583,0976-2833 VOL14, ISSUE6, 2023

- Patients with chronic inflammatory diseases, renal or liver failure.
- Patient not willing to take part in the study

3. METHODS

A single contiguous keloid per patient was considered for the study. Keloids in Group TAC received intralesional TAC 40 mg/mL, keloids in Group 5-FU received intralesional 5-FU 50 mg/mL, and those in Group T + F received intralesional injection of a combination of TAC (40 mg/mL) and 5-FU (50 mg/mL) in a ratio of 1:9. The drugs used were undiluted, but for the said combination.

Injections were made with insulin syringe such that volume injected do not exceed 1 mL per square centimeter of keloid. Whenever necessary, multiple pricks were made 1 cm apart to ensure complete and uniform distribution. Injections were administered every 3 weeks till 24 weeks or till the keloid resolves.

No local infiltration of anesthetics was done; analgesic was administered orally. Patients received no other therapies like scar massage, laser therapy, or pressure garments during the course of study. All patients were evaluated before every injection and a final evaluation was performed 24 weeks after first dose.

For VSS, keloid height was measured with scale; pliability was assessed by palpation; vascularity was assessed by visual inspection; and pigmentation was scored after blanching and comparing it with the surrounding skin. Blanching was achieved using a piece of clear plastic sheet. A p-value of <0.05 was considered to be significant.

4. RESULTS

Table 1: Demographic details

	Group A		**Group B**		**Group C**	
	N	**%**	**N**	**%**	**N**	**%**
Gender						
Male	10	50	4	70	10	50
Female	10	50	6	30	10	50
Age (In Years)						
18-30	10	50	14	70	4	20
31-40	8	40	6	30	10	50
41-50	2	10	0	0	6	30
Site						
Chest	16	80	4	70	14	70
Back	2	10	4	20	4	20
Arm	2	10	2	10	2	10
Etiology						
Spontaneous	6	30	10	50	4	20
Traumatic	14	70	10	50	12	20
Infective	0	0	0	0	4	60
Family History						
Yes	0	0	2	10	2	10

ISSN: 0975-3583,0976-2833 VOL14, ISSUE6, 2023

No	20	100	18	90	18	90

Male and female in group A and C are 50% each and in group B there are 70% males and 30% females. 47% of patients belonged to age group of 18- 30, 40% in age group of 31-40 and 13 % over 41 years. among study groups with 74% patients having keloid on chest and 16 % on back and 10% on arm. Among study groups where in traumatic etiology was more common with 70% of patients in group A, 50% patients in group B and 60% patients in group C followed by spontaneous and infective etiology. 2 patients from group B and group C having positive family history positive.

Table 2: Height (vancouver scar scale) among the study groups

Height	**Group A**		**Group B**		**Group C**		**p value**
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Baseline	1.40	0.52	1.60	0.56	1.40	0.54	0.23
6 weeks	1.40	0.52	1.60	0.57	1.20	0.44	0.18
12 weeks	0.60	0.48	0.80	0.47	0.40	0.55	0.11
24 weeks	0.15	0.06	0.20	0.42	0.12	0.07	0.32
Improvement in	89.29		87.5		91.43		
Score (%)	<0.01*		0.002*		0.018*		

According to Vancouver scar scale with maximum improvement in group C from mean height of 1.40 to mean value of 0.12 after 24 weeks.

Table 3: Vascularity and pliability (vancouver scar scale) among the study groups

Vascularity	**Group A**		**Group B**		**Group C**		**p value**
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Baseline	2	0.59	2.40	0.53	2.40	0.56	0.58
6 weeks	1.80	0.45	1.20	0.45	1.80	0.47	0.37
12 weeks	1	0.73	0.60	0.51	0.60	0.55	0.14
24 weeks	0.13	0.07	0.18	0.09	0.10	0.08	1
Improvement in Score (%)	93.5		92.5		95.83		
p value	<0.01*		0.001*		<0.01*		

ISSN: 0975-3583,0976-2833 VOL14, ISSUE6, 2023

Pliability	**Group A**		**Group B**		**Group C**		**p value**
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Baseline	4.20	0.86	4.0	1.0	4.20	0.84	0.71
6 weeks	2.80	1.09	3.2	1.09	2.60	0.89	0.16
12 weeks	1.80	0.84	2.6	0.89	1.40	0.55	0.07
24 weeks	0.56	0.41	0.80	1.08	0.54	0.47	0.09
Improvement in Score (%)	86.67		80		87.14		
p value	<0.01*		<0.01*		<0.01*		

According to vancouver scar scale with mean baseline value of group A, B and C as 2±0.59, 2.40±0.53 and 2.40±0.56 improving to 0.13±0.07, 0.18±0.09 and 0.10±0.08 respectively after 24 weeks. According to vancouver scar scale with mean baseline value of group A, B and C as 4.20±0.86, 4±1.0 and 4.20±0.84 improving to 0.56±0.41, 0.80±1.08 and 0.54±0.47 respectively after 24 weeks with maximum improvement in group C.

Table 4: Pigmentation (vancouver scar scale) among the study groups

Pigmentation	**Group A**		**Group B**		**Group C**		**p value**
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Baseline	1.60	0.55	1.60	0.55	1.60	0.52	0.94
6 weeks	1	1	1.60	0.57	1.60	0.55	0.10
12 weeks	0.20	0.39	1.60	0.58	1.40	0.89	0.039*
24 weeks	0.20	0.39	0.20	0.31	0.40	0.82	0.034*
Improvement in Score (%)	87.5		87.5		87.5		
p value	<0.01*		<0.01*		<0.01*		

Pigmentation grading according to vancouver scar scale with mean baseline value of group A, B and C as 1.60±0.55, 1.60±0.55 and 1.60±0.52 improving to 0.20±0.39, 1.2±0.31and 0.40±0.82 respectively after 24 weeks.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE6, 2023

Table 5: Overall VSS score among the study groups

Overall VSS	**Group A**		**Group B**		**Group C**		**p value**
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Baseline	9.6	0.67	9	0.58	9.8	0.71	0.13
24 weeks	0.25	0.24	0.32	0.29	0.33	0.48	0.18
Improvement in Score (%)	97.40		96.44		96.33		
p value	<0.01*		<0.01*		<0.01*		

Maximum improvement was seen in Group C then Group A and then Group B.

Table 6: Complications

Complications	**Group A**		**Group B**		**Group C**	
	N	**%**	**N**	**%**	**N**	**%**
Telangiectasia	6	30	0	0	0	0
Skin Atrophy	6	30	0	0	2	10
Hypopigmentation	8	40	0	0	0	0
Ulceration	0	0	8	40	2	10
Systemic Side Effects	0	0	0	0	0	0
Pain	2	10	8	40	0	0
P Value						
A Vs B	0.07					
A Vs C	0.021					
B Vs C	0.039					

In Group A telengiectasia, skin atrophy and hypopigmentation was seen whereas ulceration and pain was more common in Group B. There were no systemic side effects.

5. DISCUSSION

A total of 60 patients were enrolled in the study and were randomly distributed in three groups of 20 each where Group A received intralesional triamcinolone, Group B received intralesional 5 FU and Group C received combination of both. The youngest patient included in the study was 19 years old and the oldest was 45 years old where 28 patients (46%) were in age group of 18-30 years signifying greater apprehensions regarding physical appearance

ISSN: 0975-3583,0976-2833 VOL14, ISSUE6, 2023

in the younger age group. There were 26 females (43%) and 34 males (57%) in the study with 60 patients.

The therapeutic response in each parameter has been assessed. The study done by Margaret Shanthi et al[15] showed a significant reduction in pigmentation by the 3rd week. In our study there was a significant change in pigmentation by the 6th week. The study conducted by Manuskiatti et al[16] showed a significant change in pliability by 8 weeks and the study by Margaret Shanthi et al[15] had shown a significant change in pliability as early as 3 weeks. There was a significant change in pliability by 6th week in our study. There was an improvement of 86.67% in pliability score. Vascularity was assessed by visual inspection which showed significant change by 12 weeks with improvement in score of 93.5%. The study conducted by Darougheh A et al[17] has shown that only 20% of the patients showed complete flattening by 12 weeks.

In this study group none of them showed complete response with regard to pigmentation. A significant change in pigmentation was observed after 12th week. None of the patients showed complete response by the end of 24 weeks also. The study done by Manuskiatti et al[16] showed a significant reduction in pliability by 16 weeks when compared to our study where it was found to be 12 weeks. There was 80% improvement in pliability score of patients. Vascularity on visual inspection showed significant improvement by 6 weeks. The study conducted by Kontochristopoulos et al[18] has shown that hyperpigmentation and pain after injection were seen in 100% of the patients. Hyperpigmentation in 14 (70%) patients and pain immediately after injection in 8 patients (40%) were observed in our study.

A significant change in pigmentation was noted after the 12th week. The study conducted by Manuskiatti et al[16] has shown a significant change in pliability by 8 weeks when compared to our study where it was seen by 6 weeks. This may be due to the fact that a lower concentration of Triamcinolone (20mg/ml) was used by them and the time interval between the doses was increased to 4 weeks in the last two treatments. Vascularity showed a significant change after 6 weeks with improvement of score by 95.83%. Regarding the side effects observed in this group, hypopigmentation and skin atrophy. Atrophy was seen in 2 patients (10%). Ulceration was seen in 10% patients. This is lower when compared to that observed in the patients treated with Triamcinolone or 5FU alone. In my study Triamcinolone acetonide (TAC), 5-fluorouracil (5FU) and their combination were all effective in keloid scars. A combination of TAC +5FU seems to offer the balanced benefit of faster and more efficacious response with lesser adverse effects when compared to individual drugs. Treatment has to be individualized and can be combined with one or more modalities to aim for better efficacy and safety.

6. CONCLUSION

In our study the prevalence of keloids was found to be more in males than females. The majority of keloids were seen in the 18 to 40 years age group in our study. Etiology was divided into “infective,” “traumatic,” and, if there was no discernible etiology, “spontaneous. The maximum number (56%) of patients had traumatic etiology for development of keloids in our study. The other common etiology observed was spontaneous and infective in the descending order of frequency. Decrease in pigmentation was significantly faster with Triamcinolone. Telangiectasias and skin atrophy were seen most commonly in TAC group, while skin ulceration was a common problem in 5FU group.

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ISSN: 0975-3583,0976-2833 VOL14, ISSUE6, 2023

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