Section: Skin & Venereal Diseases

Original Research Article

COMPARISON OF INTRALESIONAL 5-FLUOROURACIL AND INTRALESIONAL 5-FLUOROURACIL WITH TRIAMCINOLONE ACETONIDE IN TREATMENT OF KELOIDS: A HOSPITAL BASED STUDY

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Abstract

Background: Keloidal scarring is one of the most frustrating clinical problems in wound healing. They remain a therapeutic problem in these days. Keloids may follow local skin trauma or inflammatory skin disorders like laceration, tattoos, burns, injections, ear-piercing, vaccination, bites, acne, abscess or surgery. There is no universally accepted treatment modality resulting in permanent keloid scar ablation. Multiple modalities of treatment have been advocated Hence, searching for the best modality for treating keloid and improving cosmetic acceptability is necessary. **Materials and Methods:** The study was conducted in the post-graduate department of Skin & Venereal Diseases, S.C.B. Medical College & Hospital, Cuttack, Odisha from October 2012 to September 2014. The sample size for the study was 60 patients who were divided into two groups. The patients were selected and randomly divided, with one group subjected to intralesional 5-fluorouracil (5-FU) and the others given intralesional 5-fluorouracil with Triamcinolone acetonide. **Result:** In this study there was female preponderance. About 2/3rd patients had keloids of ≤5years duration. Pruritus was the commonest presenting symptom seen in 67% of the patients. Trauma was the commonest predisposing factor observed in 41% of the patients followed by infection in 35% of patients. Family history of keloid was present in only 8% of the patients. Chest was the commonest site (60%) followed by upper extremity (15%). In group A (intralesional 5-fluorouracil), excellent response was seen in 33 % of the patients. In group B (intralesional 5-fluorouracil with triamcinolone acetonide), excellent response was seen in 52% of the patients. **Conclusion:** Combining 5-FU & TAC has a better response rate than 5-FU alone. Recurrence was not seen in both the groups and lesions less than 5 years duration responded well than lesions more than 5 years old. The Patients demographic profile and site of lesion had no significance in the outcome.

INTRODUCTION

Keloidal scarring is one of the most frustrating clinical problems in wound healing.[1–3] They remain a therapeutic problem in these days. Keloids may follow local skin trauma or inflammatory skin disorders like laceration, tattoos, burns, injections, ear-piercing, vaccination, bites, acne, abscess or surgery.[4–7] Medical advice is sought for relief of pruritus, pain, restricted movement, and mainly for cosmetic disfigurement.[8–10]

Keloid is a firm, irregularly shaped, thickened, hypertrophic, fibrous pink, red excrescence presents as extremely tender, painful, pruritic lesion. They may be single or multiple and of varying sizes.[11,12] Keloids may appear later and proliferate indefinitely and invade adjacent normal dermis. Collagen fibers in keloids are larger, thicker and wavier and assume

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a random orientation. Keloids have increased fibroblast proliferation rates.[4,7]

Treatment modalities for keloids include: 1) Compression garments, 2) Radiation, 3) Surgical Excision, 4) Intralesional injections, 5) Cauterization, 6) Cryotherapy, 7) Laser surgery, 8) Silicone gel dressings.[1,6,13–15] There is no universally accepted treatment modality resulting in permanent keloid scar ablation. Multiple modalities of treatment have been advocated. Most of the above modalities have a variable and transient success. Hence, there is a need to search for the best modality for the treatment of keloid and improve cosmetic acceptability.[1,6,13–15] Intralesional triamcinolone is the most widely used treatment for keloids and has remained the first line treatment for keloids. And, 5-fluorouracil is being considered another option for treatment strategy of keloids. Intralesional 5-fluorouracil has been used successfully as monotherapy as well as in combination with intralesional corticosteroids to treat hypertrophic scars and keloids.[1,6,13–15] Therefore, intralesional triamcinolone acetonide and intralesional 5-fluorouracil is chosen in this study. Aim of the study was to observe and compare the clinical response of intralesional 5-Fluorouracil alone and intralesional 5-Fluorouracil with Triamcinolone acetonide in treatment of keloids.

MATERIALS AND METHODS

The study was carried out in the Post-graduate department of Skin & Venereal Diseases, S.C.B. Medical College & Hospital, Cuttack, Odisha from October 2012 to September 2014. The sample size for the study was 60 patients who were divided into two groups. The patients were selected and randomly divided and the patients with an odd number were subjected to intralesional 5-fluorouracil (5-FU) and the even number ones were given intralesional 5-fluorouracil with Triamcinolone acetonide. For this study, ethical clearance was obtained from ethical committee of S.C.B. Medical College & Hospital, Cuttack.

Patients with keloids meeting the inclusion criteria were included in the study. Written consent for their participation in the study & treatment were taken. Patients were informed that 5-fluorouracil is primarily an anticancer agent. Detailed history of predisposing factor, symptoms, duration, site, family history and evolving dermatoses was recorded. Investigations like liver function test, Complete blood count, blood urea & creatinine were carried out for each subject. Skin test with lignocaine was done using 0.1 ml of 1% lignocaine solution in an insulin syringe administered intradermally. Clinical observation and recording of finding at subsequent visit and at the end of 12th visit were done and the same is followed up after 3 & 6 months of completion of therapy. The clinical assessment of scar was done based on the Patient and Observer Scar Assessment Scale.

Inclusion Criteria

All patients with keloid not received any kind of treatment or intervention before commencement of this study.

Exclusion Criteria

Pregnancy and lactation

Patients with systemic illness uncontrolled hypertension, diabetes, mental disorder, malignant tumors

Patient not willing for follow up after initial visit

Patient under 12yrs of age

Numerical data analysis was done for age, sex, duration, site, predisposing factor, presenting complain, family history. Categorical data analysis was done by using Chi-square test between two groups to correlate between the groups. P-value of 0.05 or less was considered for statistical significance. P-value of more than 0.05 was considered for statistical non-significance. Statistical analysis was done using SPSS software.

RESULTS

Out of 60 patients 30 patients (Group A) receiving intralesional 5-fluorouracil (5FU) and 30 patients (Group B)- Intralesional 5-fluorouracil with triamcinolone acetonide (5FU+TAC) were observed and the result were tabulated and analyzed statistically.

Age range was 11-50years. Least number of patients were seen in age group 41-50 years. Out of 60 patients, 33(55%) were females and 27(45%) were males. Male to female ratio was found to be 1:1.2. In majority of patients the duration of lesion was ≤5 years (73%) followed by >5years (27%). The range of duration of lesions was 6 months to 10 years. [Table 1]

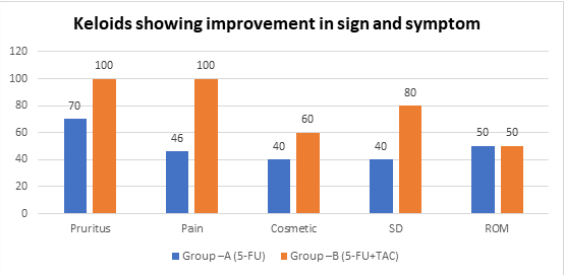

Figure 1: Keloids showing improvement is signs and symptoms

In group B(5FU+TAC) good to excellent result was seen in 96% as compare to group A (5FU) it was 73% .And fair response was seen in 17% in group A(5FU) where as in Group B(5FU+ TAC) fair response was seen only 4% cases. No poor response was seen in group B (5FU +TAC).

In Group A, improvement in pruritus was seen in 70% of patients, followed by restriction of movement in 50%, pain improved in 46% and 40% patients had improvement in cosmetic appearance and skin discoloration. In Group B, 100% improvement was

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seen in pruritus and pain, 80% of patients had improvement in skin discoloration followed by 60% in cosmetic appearance and 50% had improvement in restriction of movement.

Patients with ≤5years of duration of lesion showed excellent response in 20 (45%) patients, 21(48%) showed good response, only 1(2%) showed poor response. The difference in overall response depending on duration of lesion was found to be significant ($p<0.05$). [Table 3]

Immediate complication: All patients experience immediate pain at site of injection. Erythema was also seen in all patients. 6(20%) in Group A (5FU) and 3(10%) in Group B (5FU+TAC) had ulceration at the site of injection which healed with the use of topical antibiotics in 2-3 weeks in all cases. No systemic side effect was noted in any patients. [Table 4]

Out of 22 patients only 2 patients had mild pruritus without any signs of recurrence in 5FU group. In 5FU+TAC no signs of recurrence or reappearance of the symptoms was observed. 45 (75%) (21 in Group A 5FU and 24 in Group B 5FU+TAC) patients came for follow up at end of 6 month of completion of therapy. No signs of recurrence or reappearance of the symptoms was observed in both the groups. [Table 5]

Table 1: Socio-demographic characteristics for study participants

Characterstics		**Group A (5- FU)**	**Group B (5FU+TAC)**	**Total**	**Percentage**
Age Group (years)	11-20	9	7	16	27
	21-30	15	15	30	50
	31-40	5	6	11	18
	41-50	1	2	03	5
Gender	Male	13	14	27	45
	Female	17	16	33	55
Duration of lesion	≤5 years	20	24	44	73
	>5 years	10	6	16	27
Family History	Present	2	3	5	8
	Absent	28	27	55	92

Table 2: Comparison between group a 5-fu and group b 5-fu+tac at the end of treatment

Clinical Response	**Group A (5-FU)**	**Group B (5-FU+TAC)**	**Total**	**Percentage**
ER	10	16	26	43
GR	12	13	25	42
FR	5	1	6	10
PR	3	0	3	5
Total	30	30	60	100

Table 3: Clinical response in relation to duration of Keloid

Response	**≤5 years duration**		**>5 years duration**	
	Number	**Percentage**	**Number**	**Percentage**
ER	20	45	6	38
GR	21	48	4	25
FR	2	5	4	25
PR	1	2	2	12
Total	44	100	16	100

Table 4: Complications of 5-fu & 5fu+tac in relation to duration of the treatment

Complications	**Group A (5FU)**					**Group B (5FU+TAC)**				
Side effect	**No. of patients**	**1st day**	**2nd day**	**Delayed (2-6 months)**	**%**	**No. of patients**	**1ST day**	**2nd day**	**Delayed (2-6 months)**	**%**
Pain	30	+	_	_	100	27	+	_	_	90
Erythema	30	+	_	_	100	30	+	_	_	100
Ulceration	6	_	+	_	20	3	_	+	_	10
Hyperpig.	27	_	_	+	90	_	-	_	_	_
Hypopig.	-	-	-	-	_	2	-	_	+	7
Atrophy	-	-	-	-	_	1	-	_	+	3
Telangiectasia	-	-	-	-	_	1	-	_	+	3

Table 5: Follow up at 3 months of completion of treatment

No of patients	**Group A (5FU)**		**No of patients**	**Group B (5FU+TAC)**	
	Signs of recurrence	**Reappearance of the symptoms (pain , pruritus)**		**Signs of recurrence**	**Reappearance of the symptoms (pain, pruritus)**
20	_	_	26	_	_
2	_	+	0	_	_
22			26		

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DISCUSSION

In this study 50% of patients belonged to the age group of 21-30 years followed by 27% patients in the age group of 11-20 years. The age range was 15 -50 years. More 70 % of patients were within age of 30 years. Ketchum et al found that keloids usually occur in patients less than 30 years of age group, because youngsters are frequently subjected to trauma.16 There is more tension in younger skin and the collagen synthesis rate is higher in younger individuals. Out of 60 patients, 55% were females and 45% were males. Male to female ratio was found to be 1:1.2. This is in accordance with earlier studies by Cosmon et al.[17] Ketchum et al found almost equal incidence among both males and females. In this study the higher incidence in females probably reflected a greater cosmetic concern about keloids.[16,18,19]

In 73% of patients the duration of lesion was ≤5 years and >5years in 27% of patients. Cosman et al in their study observed that most of the keloids occurred within 1 year of local trauma and others as early as to 2-4 weeks.[17,20] In this study the longer duration of the lesions can be attributed to the negligence on the part of patients.

Out of 60 patients, 67% patients had complaint of pruritus, 42% patients had pain and cosmetic disfigurement was noted in 33% patients. 17% patients had skin discoloration and 7% patient presented with restriction of movements. In Brian et al study presenting signs and symptoms were pruritus, pain, cosmetic disfigurement, skin discoloration and restriction of movements.[1] In Nanda et al study itching was in 64.3%, pain in 21.4%, cosmetic reasons in 21.4% and restriction of movements in 7.1%.[21]

Our observation in this study coincided with earlier studies. In this study, the common site of keloids was chest in 60%, followed by upper extremity 15%, shoulder and back 10%. Least common site was leg 2%. According to Brian et al study the most common sites for keloids were chest, shoulders, head-neck areas, arms and upper back.1 Muir in his study found higher incidence of keloids over pre-sternal area followed by deltoid and ear. Bayat et al found that keloids occur most commonly on chest, shoulder, upper back , nape of neck and ear lobes. Our study very well coincided with earlier studies.[22,23]

In this study, the primary outcomes evaluated were the percentage of decrease in keloid height, pliability and relief of symptoms as the efficacy parameters. The two groups were comparable with respect to age, sex, site and duration of lesion, with statistically no significant difference ($p>0.05$). Out of 30 patients, excellent response was seen in 10 (33%) patients, 12(40%) patients showed good response, followed by fair response in 5 (17%) patients and 3 (10%) patients showed poor response. In Nanda et al study majority of patients i.e., 71.4% patients showed good response, followed by 14.3% fair response, 7.1% excellent response and 7.1% showed poor response.[21] In Gupta et al study, out of 24 patients 8(33%) patients showed excellent response, 6(25%) patients showed good response and fair response.[24] 4(16.6%) patients showed poor response. Kontochristopoulos et al in his study found that out of 20 patients, 17(85%) patients showed more than 50% improvement.[25] In Sharma study excellent response was seen in 32% of lesions while poor response was seen in 12% of lesions.[26]

Out of 30 patients in16 (52%) excellent response was seen and 13(44%) patients showed good response and fair response in 1(4%). None of the patients showed poor response. Our results were similar to Sharma study. Our results were consistent with the study by Wu et al which showed an efficacy of 97.14%. The results of our study were comparable with those reported previously by Davidson et al.[27,28]

In group B(5FU+TAC) good to excellent result was seen in 96% as compare to group A (5FU) it was 73%. And fair response was seen in 17% in group A(5FU) where as in Group B(5FU+ TAC) fair response was seen only 4% cases. No poor response was seen in group B (5FU +TAC). Combination of 5FU +TAC showed better results as compare to 5FU alone ($p<0.05$). Our results are consistent with Sharma study in which good to excellent result was seen in 96% in 5FU+ TAC and in 5FU alone it was 73% and Wu et al which showed an efficacy of 97.14%.26,27 The results of our study were comparable with those reported previously by Davidson et al.[28]

KEL In Group A, improvement in pruritus was seen in 70% of patients, followed by restriction of movement in 50%, pain improved in 46% and 40% patients had improvement in cosmetic appearance and skin discoloration. In Group B 100% improvement was seen in pruritus and pain, 80% of patients had improvement in skin discoloration followed by 60% in cosmetic appearance and 50% had improvement in restriction of movement.

According to Sharma study improvement in pruritus, pain, cosmetic appearance, restriction of movement was better in 5FU+TAC group than 5FU alone, results similar to our study.26 Patients with ≤5years of duration of lesion showed excellent response in 20 (45%) patients, 21(48%) showed good response, only 1(2%) showed poor response. The difference in overall response depending on duration of lesion was found to be significant ($p<0.05$). Ketchum et al in his study with triamcinolone acetonide for treatment of keloid and hypertrophic scars found that lesions of younger duration (<2years) were more responsive to treatment than the lesions of longer duration.16 In Gupta et al study with 5- fluorouracil for treatment keloid found that lesion of ≤5 years duration in 54.5% excellent response was seen while in 15.4% of patients of duration > 5 years excellent response was seen.[29]

Immediate complication: All patients experienced pain at site of injection. Erythema was also seen in all patients. 6(20%) had ulceration at the site of injection

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which healed with the use of topical antibiotics in 2-3 weeks in all cases. No systemic side effect was noted in any patients. Delayed complication (2-6 months): In 27(90%) patients, hyperpigmentation was seen. In study by Nanda et al, pain at injection site was seen in 100%, ulceration in 21.4% and burning sensation in 7.1%. Ulceration healed with topical antibiotics in 2-3 weeks.[21] In Gupta et al study, almost all patients experienced pain and hyperpigmentation at site of injection. One patient develop ulcer at site of keloid which healed completely within 4 weeks of time with metronidazole gel dressing.[24,29]

Immediate complication: Pain was seen at site of injection in 27(90%). Erythema was also seen in all patients. Ulceration was seen with 3(10%) of patients. Delayed complication (2-6 months): hypopigmentation 2(7%), atrophy 1(3%), telangietasia 1(3%) was seen. Similar results with Sharma study, 3(12%) showed atrophy, 2(8%) had hypopigmentation, 1(4%) developed hyperpigmentation and 1(4%) showed telangietasia.[26]

In both group incidence of adverse effects was statistically non-significant ($p>0.05$). 48(80%) [22 in Group A (5-FU) and 26 in Group B (5FU+TAC)] out of 60 patients came for follow up for 3 month after the discontinuation of therapy. Out of 22 patients only 2 patients had mild pruritus without any signs of recurrence in 5-FU group. In group B, no signs of recurrence or reappearance of the symptoms was observed. 45 (75%) [21 in Group A 5FU and 24 in Group B (5FU+TAC)] patients came for follow up at end of 6 month of discontinuation of therapy. No signs of recurrence or reappearance of the symptoms was observed in both the groups at the end of 6 month follow up. Our results were similar to that of Nanda et al, Gupta et al, Sharma study.[21,26,29] Study limitation: This study consisted of a smaller sample size i.e. 60 keloid lesions. Further studies with larger sample sizes may provide us a better and accurate understanding regarding the treatment of keloids.

CONCLUSION

Combining 5-FU & TAC has a better response rate than 5-FU alone. Recurrence was not seen in both the groups and lesions less than 5 years duration responded well than lesions more than 5 years old. The Patients demographic profile and site of lesion had no significance in the outcome.

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