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ORIGINAL RESEARCH

Treatment Approach to Non-responsive Keloid: Our Experience

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Keloid, Triamcenolone acetonide, 5-FU, Non-responsive keloid.

ABSTRACT

Keloids are abnormal scars, which are extremely distressing for the patients. Pain and itching are the two most cumbersome complaints which affect a patient's life in multiple ways. Keloids are irregular growth, which looks ugly, if present over exposed areas. Cosmetic, physiological and psychosocial aspects are compromised and patients avoid social gatherings and may undergo severe depression. Although there are multiple treatment modalities for keloids like intralesional injections of steroids, cytotoxic drugs, cryotherapy, radiation therapy, surgical excision, etc. but no modality is proven to be superior and effective. However intralesional injection of triamcinolone acetonide is widely practiced. Triamcenolone acetonide might not be effective, since many patients return with complaints of recurrence, non-responsiveness or unsatisfactory response. The present study shows a series of patients who underwent intralesional injection of triamcinolone acetonide but they did not respond to it. We combined intralesional injection of triamcinolone acetonide along with 5-FU. The response was satisfactory and significant improvement was noticed.

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INTRODUCTION

Keloids are abnormal scars, which are formed due to excessive scarring. Practically keloid can occur after any injury to the skin, which heals either by primary or secondary intention. The most common causes are surgical sites, trauma, burns, insect bite, body piercing etc. Although keloid can occur at any site on the body, but most common sites are the chest, ear, shoulder etc.

Term "cheloide" was coined by Alibert in 1806 from greek "chele" meaning crab's claw-to describe the lateral growth of tissue into unaffected skin. Keloids are more common in darker-skinned people as compared to white skin. Also, keloids are more common in age group 10 to 40 years as compared to extreme ages.

Keloid is a distressing problem for the patients and treating doctors especially because of its poor responsiveness nature to available treatment modalities and high recurrence rate even after surgical excision. They can hurt with a needle-like pain, itch, become ulcerated and cause psycho-social problems to the patients.[1]

PATHOPHYSIOLOGY

Wound healing is a process which completed with the help of various growth factors. The exact cause of the occurrence of keloid is not known, but it is believed that abnormal production or deficiency of growth factors, abnormal formation and conversion of collagen, and various immune and genetic factors are responsible for the formation of keloid.[2]

PROBLEMS CAUSED BY KELOIDS

Cosmetic- if keloid occurs on exposed surfaces on the body, it is highly un-aesthetic and unacceptable to patients, especially female patients. keloid causes irregular unsightly swelling which is noticed from a distance. Keloids are rarely camouflageable, hence

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patients affected with keloid visit multiple clinicians in an attempt to receive treatment.

Physiological- keloid are very painful. Many times, keloids cause severe, intense, and long-lasting pain, which is not relieved without medication. If the keloid is formed at movable surfaces like the eyelid, oral commissure, nasal ala, across the joint, etc., it causes restriction of movement of affected body part. Ulcerated keloid can cause local as well as systemic infection and seropurulent discharge.

Psycho-social- patients with large, exposed, and unresponsive keloid suffer from depression, low self-esteem, avoidance of social gatherings, and even suicidal tendencies.[3-5]

Keloid is cumbersome to both the patient as well as clinician. Keloid is a condition that is not uncommon and one of the most unresponsive entities. Keloids generally show no or poor response to medical treatment and high rate of recurrence after surgical intervention.

Treatment of Keloid- since keloids are difficult to treat, hence multiple inventions and modalities have been tried from time to time. Various modalities of treatment include intralesional steroid injection, intralesional cytotoxic drugs, laser therapy, excision, radiation therapy, cryotherapy, growth factor and immune therapy, etc. Although there are various modalities, till date, no single modality is proven to be effective. However, intralesional injection of steroids, triamcinolone acetate is the most common method of treatment.[6,7]

Recently another drug used to be effective for the treatment of keloid is 5-Fluoro Uracil which causes suppression of fibroblast proliferation and angiogenesis.[8]

No modality has been proved to be ideal to date. Intralesional triamcinolone acetonide is acceptable in reducing the volume of the lesion. However, it is not proven to be an ideal and effective method. Studies for intralesional 5-FU have been conducted and found to be effective, but the combination of triamcinolone acetonide and 5-FU seems to be superior than either alone.

Intralesional 5-FU has been compared with the combination of intralesional 5-FU and triamcinolone acetonide in India. The combination was found to be superior. Intralesional triamcinolone acetonide has also been compared with the combination of triamcinolone acetonide and 5-FU in Iran but not in India. That is why this study is being done to see the effect of triamcinolone alone *vs* a combination of triamcinolone and 5-FU in our population.

A study on the combination of 5-FU and triamcinolone vs 5-FU alone, a randomized controlled trial on 50 patients in 2012 was done by Saurabh Sharma et al and the combination was found to be effective.[9]

METHODOLOGY

The present study is a case series, done on 16 patients, presented to the department.

Inclusion criteria

All patients with keloid not responding to intralesional injection of triamcinolone have been included in the study.

Exclusion criteria

Patients who had active infections with purulent discharge and skin ulceration were excluded from the study.

All patients with keloid not responding to intralesional injection of triamcinolone were included in the study from March 2023 to February 2024. Informed consent was taken from all patients. The size and characteristics of the keloid were noted. Keloid was assessed as per the Vancouver scar scale and POSAS. Patients were given intralesional injections of 0.9 mL Inj. 5-Fluorouracil 50 mg/mL + 0.1-mL of Inj. Triamcinolone 40 mg/mL reconstituted in a 1cc insulin syringe into the keloid. Intralesional injections were repeated 4 weeks apart. Injections were administered till the keloid had flattened or for a maximum of six doses. Size of the keloid, Vancouver scar scale, and POSAS reassessed after completion of treatment. Complications during the treatment period were also recorded. Patients were followed up for 4 months to watch for recurrence or symptomatic aggravation.

Outcomes parameters

Assessment was done by using the following parameters. All parameters were assessed before starting the treatment, and after completion of treatment that is maximum 6 doses.

Following parameters were seen in Patient's assessment- Pain, Itching, Scar color, Thickness, Stiffness, Irregularity, Size.

Following parameters were used in observer's assessment- Vascularity, pigmentation, thickness, pliability.

OBSERVATION

Demographic and Basic Characteristics of Keloid

The age range of our patients was a minimum 23 years to a maximum of 60 years. Females have slightly higher incidence than males, in our study, 9 patients were female and 7 patients were male. 6 patients had keloid over the ear, 6 patients had keloid over chest, 2 patients had keloid over fore arm, and 2 patients had keloid over left mandibular region. Whereas the maximum size of the keloid treated was 7x5x1 cm (Table 1).

Assessment of Keloid

Assessment was done by using two scales. Vancouver scar scale and POSAS scale.[10,11]

Vancouver scar scale included the clinician's assessment whereas POSAS scale included both patient's as well as clinician's assessment. Figure 1 shows of effect of kenacort plus 5 FU after first dose, a significant reduction in keloid size can be noted, patient is still under treatment. Both scorings were done before starting the treatment and final scoring was done after completion of the treatment. An improved trend was noticed in both scores as shown in table 2. Figure 2 shows a complete reduction of pre-sternal keloid after two injections.

Complications

None of the patients showed complications. Only one patient complained of darkening over the keloid surface, which was slight and acceptable.

Follow-up period

None of the patients showed recurrence after a 4-months follow-up and none of the patients turned with a re-appearance of symptoms like itching and pain.

DISCUSSION

Non-responsiveness nature of keloid is not uncommon. A keloid is said to be "non-responsive" when it shows no response to medical management, either with individual or combination drugs.

Although intralesional injection of TA is the most common modality for the treatment of keloid, in many cases this therapy is not effective. Due to

Table 1: Demographic characteristics of patients and basic features of keloid.

S. No	Age	Gender	Site	Size	Size of keloid (post-injection)
1	25	F	b/l ear	Rt – 0.5 x 0.5 x 0.5cm Lt – 2 x 2 x 1cm	Rt – flat Lt – 1 x 1cm
2	33	F	Lt ear	4 x 2x 1.5cm	3 x 1.5x 1cm
3	45	M	Chest	5 x 4 x0.5cm	5x3x0.2cm
4	52	M	Chest	3x2x1cm	3x1.5x0.2cm
5	38	F	Chest	2.5x2x1cm	2.5x2x0.2cm
6	46	F	Rt ear	2x2x1cm	2x1.5x0.5cm
7	22	F	Lt ear	3x3x1.5cm	3x3x1cm
8	32	M	Lt Mandibular	2x1x1cm	2x1x0.2cm
9	40	F	Lt Scapular	3x2x1cm	3x2x0.1cm
10	50	F	Chest	7x5x1cm	6x3x0.8cm
11	33	F	Rt ear	2x1.5x0.5cm	2x1.5x0.1cm
12	27	M	Lt forearm	3x1x1cm	3x1x0.2cm
13	26	F	Rt ear	1x1x0.5cm	1x1x0.1cm
14	35	M	Chest	2x2.5x1cm	2x2x0.5cm
15	23	M	Lt Mandibular	1x1x0.5cm	1x.5x0.2cm
16	60	M	Chest	12x2x0.8cm	12x1.5x0.4cm

Figure 1: Almost 50% reduction noticed after the first dose of Kenacort plus 5 FU.

Figure 2: Complete reduction of pre-sternal keloid after three doses of injections.

associated complications of TA, Prolonged use is not recommended. intralesional injection of TA should be stopped if there is no response after 5 to 6 doses of treatment. Various local adverse effects after prolonged and overuse include hypopigmentation, ulceration, dermal atrophy, etc.

For these reasons, we have included only those keloids in our study, which did not respond to any of the conservative treatments, especially TA. Another reason is that the local and systemic effects of TA will be reduced if we combine TA with 5 FU.[12]

The present study included 16 patients with non-responsive keloids, which were recalcitrant and problematic. The study conducted by Darougheh *et al.* included a comparison of two modalities for the treatment of keloid. They divided the

Table 2: Pre- and post-injection assessment parameters..

S No	Vancouver scar scale	POSAS observer score/ overall opinion	Doses	Vancouver scar scale (post-injection)	POSAS observer score/overall opinion	Complication
1	6	27/7	5	5	23/7	Nil
2	11	50/9	6	10	45/9	Nil
3	5	52/8	3	4	45/7	Nil
4	6	48/7	5	4	40/6	Nil
5	5	45/7	5	3	35/6	Nil
6	6	50/8	6	3	44/7	Nil
7	8	47/8	6	6	41/7	Darkening
8	7	38/7	6	5	30/6	Nil
9	6	42/6	6	3	35/5	Nil
10	8	45/8	4	7	40/7	Nil
11	5	48/8	5	2	38/8	Nil
12	7	30/7	5	4	22/6	Nil
13	5	33/7	5	2	22/6	Nil
14	7	45/7	6	4	38/6	Nil
15	5	35/7	5	3	25/8	Nil
16	8	45/8	6	4	40/7	Nil

patients into two groups. Group A was treated by intralesional injection of TA, and group B was treated by intralesional injection of TA plus 5 FU. They compared the outcomes in both groups. They found that the combination drug group showed better response than single drug modality. However, they included previously untreated kinds of keloids too. But in our study, previously treated and non-responsive keloids were more focused. [13]

Another study was done by Saha *et al.*, where they compared TA with TA plus 5 FU. They also showed that 5-FU had better response as compared to TA alone. Especially hyperpigmentation, superficial ulceration, and pain were reduced in TA plus 5 FU group.[14]

Khan *et al.* also concluded that combination therapy is better than single-drug therapy. They compared intralesional TA with intralesional TA with 5-FU.[15]

A study done by Kumar S et al. included a comparative study on patients with keloids. They compared two treatment groups. Group receiving combination treatment with triamcinolone acetate with 5 fluorouracil showed better results than the group receiving triamcinolone acetate alone.[16]

All previous studies were done on keloids at different locations. None of the studies was done to see the response in case of previously failed treatment. Our study is a single study in its type. Since non-responsiveness of keloid is extremely distressing for the patient as they lose hope and become exhausted. Also, many patients suffered from local side effects of pronged use of injection kenacort.

In our study the clinical assessment as well as patient's response, both were found to be better. Another significant factor found in our study was patient compliance. Generally after a failed response to the treatment, patients get demotivated and hence their compliance becomes poor. In contrast to this, our study showed better compliance to the treatment as patients were satisfied seeing the positive response. There was no discontinuation of treatment and loss of follow-up.

The findings in this study indicate that for treatment of non-responsive keloid, combination therapy with injection kenacort and 5 FU is better than repeating the injection kenacort.

RESULT

Our study shows a good response to combination therapy with injection kenacort and 5 FU in patients with non-responsive keloids. Symptoms like pain, itching, surface ulceration, discharge, etc. were better

managed by combination therapy. The patient's compliance with the treatment was excellent, as none of the patients discontinued the treatment.

CONCLUSION

Intralesional injection of triamcinolone acetonide in combination with 5 FU shows better response in previously treated but non-responsive keloids. However, a study with a larger sample size and comparison group will be effective in drawing better conclusions.

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