International Journal of Research in Dermatology
Parmar SS et al. Int J Res Dermatol. 2022 Jan;8(1):45-49
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20214911

Original Research Article

An approach to treatment modalities of keloids: a comparative study

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Received: 30 September 2021
Accepted: 03 November 2021

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ABSTRACT

Background: In spite of the presence of such an array of treatment modalities, none of these can be claimed to be an ideal treatment option as most of them have limited efficacy, significant side effects or increased chances of recurrence. Hence the study was undertaken to search an ideal treatment for keloids which is safe, effective, and with low rate of recurrence.
Methods: Total of 200 patients were recruited out of which only 160 patients were included in study. The patients were divided into three groups and administered with different modes of treatment. Patients in all the groups were followed up at 3 weekly intervals for evaluation of response. At the end of the study, the data was compiled and analysed using appropriate statistical tests.
Results: In only 32 patients completed study in group 1, 2 and 3 respectively. Group 1, 2 and 3 were more or less equally efficacious with clearance rate. Complete clearance was seen in 24 patients in group 1 patients, in group 2 there were 22 patients with complete clearance and in group 3 there were 24 patients.
Conclusions: Intralesional triamcinolone acetonide, intralesional triamcinolone acetonide with hyaluronidase and intralesional radiofrequency with intralesional triamcinolone acetonide are almost equally effective modalities for the treatment of keloids. But, intralesional triamcinolone acetonide with hyaluronidase fares better than other two as far as safety is concerned with least side effects.

Keywords: Keloid, Intralesional injection, Treatment, Triamcinolone acetonide

INTRODUCTION

Keloids are a type of raised scar. They occur where the skin has healed after an injury. They can grow to be much larger than the original injury that caused the scar. They are not at all common, but are more likely for people who have dark skin. Anything that can cause a scar can cause a keloid. This includes being burned, cut, or having severe acne. Keloids can also develop after you get a body piercing, a tattoo, or have surgery. Keloids sometimes show up 3 months or more after your skin is injured. Some continue to grow for years.[1,2]

Keloids and hypertrophic scars are two well-known types of excessive pathologic scarring. These types differ by aesthetics, pathogenesis, histopathology, and treatment, although there are overlapping characteristics. Compared to hypertrophic scars, keloids are characterized as more clinically severe in nature, causing pruritus and pain more frequently in patients. Classically, keloid scars appear slowly over months beyond the initial wound edges, while hypertrophic scars typically develop over a period of weeks and stay within the initial edges.[3,4]

Classically, keloid scars appear slowly over months beyond the initial wound edges, while hypertrophic scars typically develop over a period of weeks and stay within the initial edges. From a histopathologic perspective, keloids include a random organization of type I and type III collagen fibers, whereas hypertrophic scars have an organized parallel pattern of type III collagen.[5] Keloids progress to form thick, firm scars that rarely heal

spontaneously, unlike hypertrophic scars that can heal unaided over years. Since keloids can be distressing to patients, there has been great interest in understanding the key aspects of keloid pathogenesis.[3]

Though keloid is essentially a benign entity but it may rarely become complicated with secondary bacterial infections, ulceration, development of malignant melanoma and basal cell carcinoma. Management of keloids has been a frustrating experience both for the treating doctors and patients. Adding to the woes, recurrent nature of keloid makes the matters worse. A number of options have been tried either alone or in various combinations with variable success.[6] In spite of the presence of such an array of treatment modalities, none of these can be claimed to be an ideal treatment option as most of them have limited efficacy, significant side effects or increased chances of recurrence. Therefore, this study was undertaken to compare various existing and newer treatment options and search for an ideal treatment for keloids which is safe, effective, and with low rate of recurrence.

METHODS

The present randomized study was done in the department of dermatology in the medical college associated with hospital. The sample size for the study was determined using G-power software. A total of 200 patients who fulfilled the inclusion and exclusion criteria were included in the study.

Any patients who were in the age range of 18 to 50 years and have diagnosed with keloids were included in the study. Patients with any medical condition, allergic to any drug, pregnant and lactating mothers were excluded from the study. The patients were explained in detail about the study. The written informed consent was taken from the included patients.

Keloids were assessed on the basis of Vancouver scar score (VSS) scoring, visual analog score-patient (VAP), visual analog score-doctor-1 (VAD-1) and visual analog score-doctor 2 (VAD-2). The dimensions of the keloid were measured using a standard ruler with centimeter markings. VSS is a universally accepted scoring system for assessment of keloids. It is a numerical scale which measures 4 variables: vascularity, height/thickness, pliability and pigmentation. The total score may vary between 0-13, with lower score showing better prognosis.

Visual analog score (VAS) is subjective ordinal scale with values ranging from 0 to 10, where 0 signifies no complaint and 10 signifies maximum complaint. VAP, VAD-1 and VAD-2 were arbitrarily taken as 10 at the start of the study. The VAS were assessed with the help of clinical photographs.

At each follow-up the patients were assessed for treatment outcomes (scar height, VSS score, VAP score, VAD-1 score, VAD-2 score) and any side-effects. All the parameters were recorded in a pre-structured proforma. Clearance was defined as reduction in height of keloid to 1 mm or less. The patients were given one of the following treatment: group-1: Intralesional triamcinolone acetonide; group-2: intralesional triamcinolone acetonide with hyaluronidase; and group-3: intralesioanl radiofrequency with triamcinolone acetonide.

Group 1

The lesion was cleaned with spirit and allowed to dry. Injection triamcinolone acetonide 40 mg/ml was injected into the lesion at appropriate depth of 3-7 mm separated by a distance of 1 cm apart using a 30 gauge insulin syringe. The total quantity administered did not exceed 2 ml/session. The procedure was repeated at 3 weeks intervals for a maximum of 8 times or until complete flattening of lesion.

Group 2

Injection hyaluronidase which is available in powder form was reconstituted with 1 ml sterilized water. Injection triamcinolone acetonide 40 mg/ml was mixed with injection hyaluronidase 1500 IU/ml in 1:1. The lesion was cleaned with spirit and allowed to dry. Mixed solution was injected into the lesion at appropriate depth of 3-7 mm separated by a distance of 1 cm apart using a 30 gauge insulin syringe. The total quantity administered did not exceed 2 ml/session. The procedure was repeated at 3 week intervals for a maximum of 8 times or until complete flattening of lesion.

Group 3

Intralesional triamcinolone acetonide 40 mg/ml was injected into the lesion at appropriate depth separated by a distance of 1 cm apart using a 30 gauge insulin syringe. 0.025-0.05 ml was injected per site. The procedure was repeated once in 6 weeks for a maximum of 4 times or until complete flattening of lesion but patients was followed up once in 3 weeks.

At the end of the study, the compiled data was analysed using the statistical tests. P value <0.05 was considered statistically significant.

RESULTS

The patients who completed the full study protocol were only included in the study. Rest were excluded from the study. Total of 160 patients were included in the study. The overall mean age was found to be 28.39±12.40 years. The average duration of keloid was found to be 4 months to 4 years. Of the total 160 patients there were 28 patients who had history of keloid in one or more of the family member. During the course of treatment there are 40 patients who were lost, were excluded from the study. The main reasons

for the dropouts were unsatisfactory treatment response, complications and change in patient's location.

Mean duration of keloids was 52.18±60.48 months in group 1, 82.06±140.19 months in group 2, 27.53±30.85 months in group 3, 44.82±35.88 months in group 4 and 43.31±40.26 months in group 5 (p value=0.33, one way analysis of variance (ANOVA) test). All groups were comparable in terms of age distribution, duration and number of keloids (Table 1).

Out of total 160 patients, there were 62 patients developed keloids without any insult, there were 48 patients who developed secondary to injury and accident, in 24 patients the keloids developed from previous acne scars and scar due to surgery was developed in 12 patients and due to miscellaneous reason the keloids were formed in 14 patients.

Owing to the treatment the complete clearance was seen in 24 patients in group 1 patients, in group 2 there were 22 patients with complete clearance and in group 3 there were 24 patients who achieved complete clearance of keloids within the study period (p value<0.001, Chi-square test).

Similarly, change in mean VSS score (from baseline to outcome) was 4.54±2.35 in group 1, 2.90±4.32 in group 2 and 3.96±2.64 in group 3. Pair wise comparison was done using schefee post hoc test, which showed no statistically significant difference in change in mean height between group 1 and group 2 (p value=0.78), group 1 and group 3 (p value=0.98), group 2 and group 3 (p value=0.93).

Change in mean VAP score (from baseline to outcome) was 8.06±1.44 in group 1, 7.94±2.57 in group 2 and 7.75±1.44 in group 3. Pair wise comparison was done using schefee post hoc test there was no statistically significant difference in change in mean height between group 1 and group 2 (p value=1), group 1 and group 3 (p value=0.87), group 2 and group 3 (p value=1).

Change in mean VAD-1 score was 7.69±2.85 in group 1, 6.98±3.26 in group 2 and 6.32±5.25 in group 3. Pair wise comparison was done using schefee post hoc test, which showed no statistically significant difference in change in mean height between group 1 and group 2 (p value=0.85), group 1 and group 5 (p value=0.78), group 2 and group 3 (p value=1).

Change in mean VAD-2 score was 7.65±2.56 in group 1, 8.24±2.23 in group 2, and 8.10±2.23 in group 3. Pair wise comparison was done using schefee post hoc test, which showed no statistically significant difference in change in mean height between group 1 and group 2 (p value=0.33), group 1 and group 3 (p value=0.24), group 2 and group 3 (p value=1).

Table 1: Various treatment modalities outcome.

Parameters	Group 1	Group 2	Group 3
Clearance rate	24	22	24
Change in VSS score	4.54	2.90	3.96
Change in VAP score	8.06	7.94	7.75
Change in VAD-1 score	7.69	6.98	6.32
Change in VAD-2 score	7.65	8.24	8.10

DISCUSSION

Keloids are elevated fibrous scars that extend beyond the borders of the original wound, do not regress, and usually recur after excision. The term is coined from the Greek word cheloides, meaning "crab's claw". Hypertrophic scars are similar, but are confined to the wound borders and usually regress over time. Keloids are raised build-ups of scar tissue on the skin. They usually form and grow after a wound, puncture, burn, or blemish. For some people, this scar tissue is more pronounced and darker than the rest of their skin tone.[2,7]

Keloids are more common in persons younger than 30 years, with risk peaking between 10 to 20 years of age, and in patients with elevated hormone levels. Sternal skin, shoulders and upper arms, earlobes, and cheeks are most susceptible to developing keloids. Keloids are more than just cosmetically unacceptable; many are also pruritic and painful. They often result in severe emotional distress.[8,9]

Corticosteroid injections for prevention and treatment of keloids and hypertrophic scars are perhaps the first-line option for family physicians. Corticosteroids suppress inflammation and mitosis while increasing vasoconstriction in the scar. Triamcinolone acetonide suspension (kenalog) 10 to 40 mg per ml (depending on the site) is injected intralesionally, which, although painful, will eventually flatten 50 to 100 percent of keloids, with a 9 to 50 percent recurrence rate. Newer keloids are more responsive to therapy than older, established lesions. Corticosteroid injections are more effective if combined with surgery; the sooner instituted, the greater the likelihood of success.[8]

Our study showed that intralesional triamcinolone acetonide, intralesional triamcinolone acetonide with hyaluronidase and intralesional radiofrequency with triamcinolone acetonide were more or less equally efficacious in the treatment of keloids with clearance rate of 73%, 66.25% and 71% respectively. Atrophy and depigmentation were seen in 10 out of 32 patients in group

1, 6 out of 32 patients in group 2 and 12 out of 32 patients in group 3. Telangiectasia was only seen with intralesional triamcinolone acetonide with 10 out of 32 patients being affected.

Ulceration and secondary bacterial infection were seen in groups using intralesional radiofrequency with 8 out of 32 patients in group 3 developing ulceration, and 2 out of 32 patients in group 3 developing secondary bacterial infection. Charring was seen in 2 out of 32 patients in group 3.

In our study, all the patients treated with triamcinolone showed good response, 24 out of 32 patients had complete clearance of keloids and there was a mean change in height by 3.15 mm. If we analyse our results vis-à-vis the reported results of the other studies done in this regard, several studies are worth mentioning here; Koc et al, in 2008, obtained an average change in height of 3.77 mm using triamcinolone acetonide alone.[10] This result is slightly better than our result of average change in height of 3.16 mm. This disparity may be attributed to the lack of differentiation between keloids and hypertrophic scars in their study.

In a recent study by Ahuja et al, published in 2013, there was complete flattening in all the patients and mean change in VSS was 7.04.[11] They had better results compared to ours which showed complete flattening in only 12 out of 16 (75%) patients and mean change in VSS of 4.12. This can be explained as both keloid and hypertrophic scars were included in their study, moreover only scars of recent onset (less than 2 years) were taken. It is a known fact that hypertrophic scar has a better prognosis than keloids.

It is known that the synthesis of hyaluronic acid in keloidal fibroblasts is more compared to normal fibroblasts. Hyaluronidase is widely used in other surgical fields to prevent and treat excessive fibrosis.[12] It is interesting to note that despite these facts no study has been described in the literature evaluating the role of intralesional triamcinolone acetonide and hyaluronidase combination in the management of keloids. Our study shows that compared to triamcinolone alone, combination of triamcinolone acetonide and hyaluronidase had similar efficacy in terms of reduction in VSS score and height but with less side effects (18.75% patients developed atrophy with combination in comparison to atrophy in 31.25% patients with triamcinolone alone, p value <0.001). But it is important to note that when triamcinolone 40 mg/ml is mixed with hyaluronidase 1500 IU/ml in 1:1 ratio, the effective concentration of triamcinolone acetonide in the mixture became 20 mg/ml.

This means there is a synergistic therapeutic effect of combination, efficacy of which is comparable to double the dose of triamcinolone acetonide used alone. It was also observed that administration of injection with combination was easier in comparison to triamcinolone acetonide alone.

Radiofrequency is a dermatosurgical procedure which has gained importance in recent years as it is highly effective in cutting of skin lesions with good hemostasis due its coagulative property. It has been recently used in the treatment of the auricular keloids.

Our study results using intralesional radiofrequency for keloids were discouraging with only 4 out of 34 treated patients having clearance and there was ulceration in 12 out of 34 patients and secondary infection in 2 out of 17 (11.76%) patients. If we analyse our results vis-à-vis the reported results of the other studies done in this regard, studies by Fruth et al can be quoted.

Fruth et al, used intralesional radiofrequency for the treatment of earlobe keloids.[13] After local infiltration of keloid with lignocaine, the radiofrequency probe was inserted into the keloid and heated to a target temperature of 70^{o} C using a radiofrequency machine set at 12 watts of power. Four out of 7 (57.14%) patients treated with only radiofrequency in patients treated with combination showed good response. Their study was uncontrolled with unequal treatment intervals and number of sittings. These results are different from our results, where and 24 out of 32 patients treated with the combination had clearance.

The relative inefficacy of only radiofrequency modality in our study, may be due to different treatment parameters used. We used monopolar ablative radiofrequency with a maximum power output of 90 watts at low to medium settings till blanching of the lesions. There are no precise guidelines for use of radiofrequency in keloids patients. The mechanism behind this novel modality is to cause dermal collagen remodelling without causing any epidermal damage as it is well known that any form of trauma is a triggering factor for keloids, especially in patients with keloidal tendency. This collagen remodelling is what was described by the previous authors as radiofrequency tissue volume reduction (RFTVR).

Klockars et al, in 2013, conducted a similar study using only intralesional radiofrequency.[14] Thirteen auricular keloids were taken for the study. After infiltration with local anaesthesia, the active electrode was directly inserted into the keloid and was heated with machine parameters of power output of 10 watts, till automatic cutoff. Only 1 sitting was performed. They reported excellent improvement in 6 out of 13 keloids, good in 5 out of 13 keloids and moderate improvement in 1 keloid. These results are different from our study where only 2 out of 17 patients (11.76%) had clearance in the form of ulceration which healed with regrowth of keloid. The difference in results can be explained due to different treatment parameters used.

Besides, it is known that ear lobe keloids have better prognosis than keloids at other areas. The results in our study were inferior to the results in studies by Fruth et al and Klochars et al, where 57.14% (4 out of 7) and 92.31% (12 out of 13) patients showed moderate to excellent

response. The difference in the results can be explained as other studies used different radiofrequency parameters and only earlobe keloid patients were included.

In our study, intralesional radiofrequency was combined with intralesional triamcinolone acetonide in an attempt to increase its efficacy. 24 out of 32 of the patients showed complete clearance. As the same radiofrequency parameters were used in both the groups, the results with the combination can probably be attributed to the effect of triamcinolone acetonide. If we analyse our results vis-à-vis the reported results of the other studies done in this regard, studies by Fruth et al and Weshay et al can be compared.[13,15]

The major limitation of this study was that our patients could not be followed up for prolonged periods after completion of the treatment, to assess the rate of recurrence and we are of the view that intralesional radiofrequency may be an effective modality. However, further attempts should be made to optimise the radiofrequency parameters to treat the keloids effectively.

CONCLUSION

Intralesional triamcinolone acetonide, intralesional triamcinolone acetonide with hyaluronidase and intralesional radiofrequency with intralesional triamcinolone acetonide are almost equally effective modalities for the treatment of keloids. But, intralesional triamcinolone acetonide with hyaluronidase fares better than other two as far as safety is concerned with least side effects.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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Cite this article as: Parmar SS, Modi A. An approach to treatment modalities of keloids: a comparative study. Int J Res Dermatol 2022;8:45-9.