Content available at: https://www.ipinnovative.com/open-access-journals

IP Indian Journal of Clinical and Experimental Dermatology

Journal homepage: www.ijced.org/

Original Research Article

A therapeutic evaluation of various modalities of treatment of keloid-A randomized open label study

Sreelakshmi T S[1], Bela B Padhiar[1,*]

[1] *Dept. of Dermatology, Venereology and Leprosy, GMERS Medical College, Gandhinagar, Gujarat, India*

ARTICLE INFO

Article history:
Received 10-04-2023
Accepted 19-06-2023
Available online 03-07-2023

Keywords:
keloid
triamcinolone acetonide
5 fluorouracil
silicone gel sheet
radiofrequency
intralesional

ABSTRACT

Background: Keloid and hypertrophic scar are the result of abnormal growth of fibrous tissue following healing of a cutaneous injury in predisposed individuals. Some treatment options are pressure garments, radiation therapy, excision, intralesional injections, cryotherapy, silicone gel dressing and lasers though no single modality is completely effective.

Aim: To study the efficacy, to compare and to study the adverse effects of 4 different modalities of treatment of keloid namely, Intralesional triamcinolone acetonide (TAC), Intralesional triamcinolone acetonide and 5-fluoro uracil (5-FU), Intralesional triamcinolone acetonide and silicone gel sheet (SGS) and Intralesional Radiofrequency (RF).

Materials and Methods: Arandomized open label study was conducted in the dermatology department of a tertiary care hospital in Gujarat from Nov 2020 to December 2022. 108 patients were allocated to 4 groups, Group 1(TAC), Group 2(*TAC* + 5FU), Group 3(*TAC* + SGS) and Group 4(RF). Group 1 received Intralesional injections of Triamcinolone acetonide (alone), Group 2 received Intralesional injections of Triamcinolone acetonide and 5- fluorouracil, Group 3 was given Intralesional injections of Triamcinolone acetonide and topical silicone gel sheet and Group 4 was treated with intralesional radiofrequency.

Results: A total of 108 patients of age group 18-52 years were enrolled and was divided into 4 groups consisting of 27 patients each**.** Improvement of pliability, vascularity, pigmentation and height of keloid was maximum in TAC + 5FU group and least was in TAC + SGS group. At the end of 4 weeks, excellent improvement was found highest in 29.6% of TAC+5FU group, 22.2% in TAC alone, 18.5% in RF group and 11.1% in TAC+SGS group. At the end of 8 weeks, excellent improvement was found highest in 51.8% of TAC+5FU group, 44.4% in TAC alone, 40.7% RF group and 25.9% in TAC+SGS group. The difference was statistically significant.Skin atrophy, telangiectasia, hypopigmentation and recurrence were observed more TAC group therapies whereas, ulceration and infection were more frequent with RF treatment, however few cases were also seen TAC+5FU group.

Conclusion: In this study in terms of pliability and overall improvement maximum response was seen in group TAC + 5 FU and TAC + SGS was least effective.

This is an Open Access (OA) journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprint@ipinnovative.com

1. Introduction

Keloid and hypertrophic scar are the result of abnormal growth of fibrous tissue following healing of a cutaneous injury in predisposed individuals, most occur between age of 10-30 years and cause morbidity.[1]

Keloids extend beyond the margins of the original wound, do not usually regress of its own, and has a tendency to recur after excision, while hypertrophic scars do not expand beyond the boundaries of the initial injury and can undergo partial spontaneous resolution.[1]

* *Corresponding author*.
E-mail address: drbelapathiar@gmail.com (B. B. Padhiar).

https://doi.org/10.18231/j.ijced.2023.018
2581-4710/© 2023 Innovative Publication, All rights reserved.

Experimental evidence implicates the importance of members of the transforming growth factor β (TGF-β) family in cutaneous scarring, as well as scarring in other organs.

There are several treatment modalities which are useful for the management of keloid, though no single modality is completely effective. Some treatment options are pressure garments, radiation therapy, excision, intralesional injections, cryotherapy, silicone gel dressing and lasers. This study is mainly dealing with efficacy of different modalities of treatment of keloid like intralesional triamcinolone, intralesional triamcinolone and 5-fluoro uracil, intralesional triamcinolone and silicone gel sheet and radiofrequency.

2. Aim & Objectives

1. To study the efficacy of various modalities of treatment of keloid and to compare them with one another.
2. To study the adverse effects of the various modalities used in the treatment of keloid.

The different modalities of treatment used in this study will be

1. Intra lesional triamcinolone acetonide.
2. Intralesional triamcinolone acetonide and 5 fluoro uracil
3. Intralesional triamcinolone acetonide and silicone gel sheet.
4. Radio frequency.

3. Materials and Method

A randomized open label study done in Dermatology department of a tertiary care hospital in Gujarat from November 2020 to December 2022. Ethics committee approval was obtained. In this randomized parallel group study, 108 patients were enrolled and randomly allocated to four groups. Written informed consent was obtained. Inclusion criteria was patients of any age and sex, keloids of size less than10 cm in the greatest dimension and duration of >6 months. Exclusion criteria were females with current pregnancy, lactating or planning pregnancy, those who have received treatment for keloids in the past 12 months,those who have active inflammation, infection or ulcer in or around the keloid and those with history of pacemaker insertion. A pre-set proforma was be used to collect patient's details. Detailed physical examination was done and investigations including CBC, RFT, LFT, HIV, HBsAg were carried out. Patients were randomly allocated to four groups. Study groups were mentioned as below:

1. Group 1: TAC – received Intralesional injections of Triamcinolone acetonide (40mg/ml) (alone)
2. Group 2: TAC + 5FU – Intralesional injections of Triamcinolone acetonide (40mg/ml) + 5- fluorouracil 500 mg/10ml, in the ratio 1:9.
3. Group 3: TAC + SGS- Intra lesional injections of Triamcinolone acetonide (40mg/ml) + topical silicone gel.
4. Group 4: RF - intra lesional radio frequency

Injections was made with 30 G insulin syringe such that volume injected would not exceed 0.5 ml per square centimeter of keloid. Whenever necessary, multiple pricks was made 1 cm apart to ensure complete and uniform distribution. A maximum of 2 ml has to be injected per session. Injections were administered every 2 weeks for a total of 4 visits, no local infiltration of anesthetics will be done.

Keloids in Group TAC will receive intra lesional triamcinolone acetonide (TAC) 40 mg/ml, and those in Group TAC + 5FU received intralesional injection of a combination of TAC (40mg/ml) and 5FU (50mg/ml) in a ratio of 1:9 every 2 weeks. Group RF was treated with intralesional radio frequency ablation every 2 weeks for a total of 4 visits with no other treatment modality was allowed. The device used was an RF generator. The device operates at approximately 4 MHz and was used with various electrodes and hand pieces to deliver RF energy to the tissue. Xylocaine sensitivity followed by Local anesthetic (1% Lidocaine) was infiltrated into the keloid and into the surrounding tissues. Intracath no 22 was used with the insulation and small nick had to be made at the base of middle and the tip of a needle to ensure a flow of current were inserted in the targeted lesion. The device had to been used with the maximal temperature of 90°C and a power output of 10 to 12 W. The mode to be used was the cut/ coagulation (blend mode). The uninsulated part of the intracath tip was needed to be inserted into the keloid, and the pre-set energy was applied to the keloid tissue until a maximal temperature of 90°C was reached. The procedure was repeated every 2 weeks for 4 visits. Patients instructed to use topical and systemic antibiotics for 1 week after the procedure.

In group TAC + SGS, after injecting triamcinolone acetonide injection, silicone gel sheet was applied over the lesion, fixed with a micropore tape and kept insitu, till the next sitting injection. In the next visit silicone gel sheet was removed, injection was given and silicone gel was re-applied. Single gel sheet can be used for 20-40 days. Each subject was evaluated at 2-week interval, after four follow- up visit final assessment was done. Treatment was carried out until keloid resolved. Vancouver Scar Scale (VSS) which includes parameters of height, pigmentation, vascularity and pliability was used for each subject. Adverse effectsat the time of injection and other complaints during the course of treatment was also be recorded.

4. Results

A total of 108 patients of age group 18-52 years were enrolled and was divided into 4 groups 27 patients each group.(Table 1)

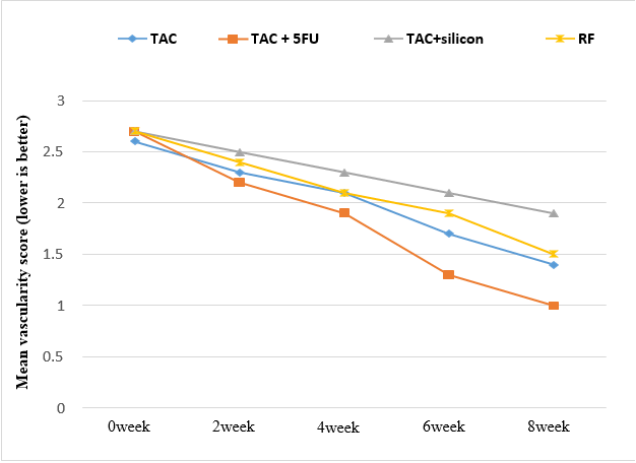

Fig. 1: Rate of change in vascularity with different modalities

The response of different treatment modalities on vascularity of keloid was best observed in TAC + 5FU group, followed by TAC alone, RF and then least was in TAC + SGS group. (Figure 1)

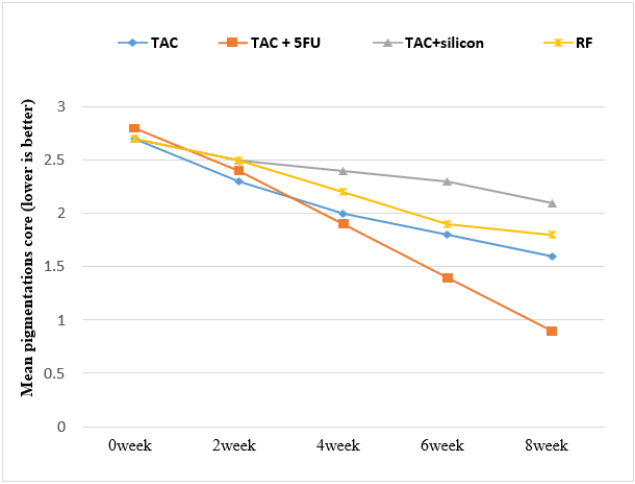

Fig. 2: Rate of change in pigmentation with different modalities

The response of different treatment modalities on pigmentation of keloid was best observed in TAC + 5FU group, followed by TAC alone, RF and then least was in TAC + SGS group. (Figure 2)

The response of different treatment modalities on pliability of keloid was best observed in TAC + 5FU group, followed by TAC alone, RF and then least was in TAC + SGS group. (Figure 3)

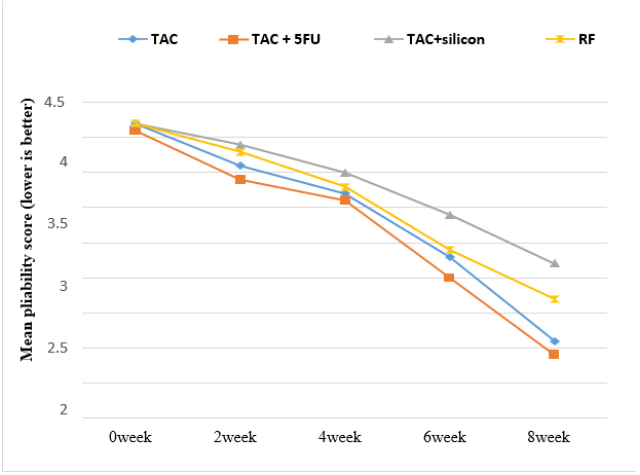

Fig. 3: Rate of change in pliability of keloid with different modalities

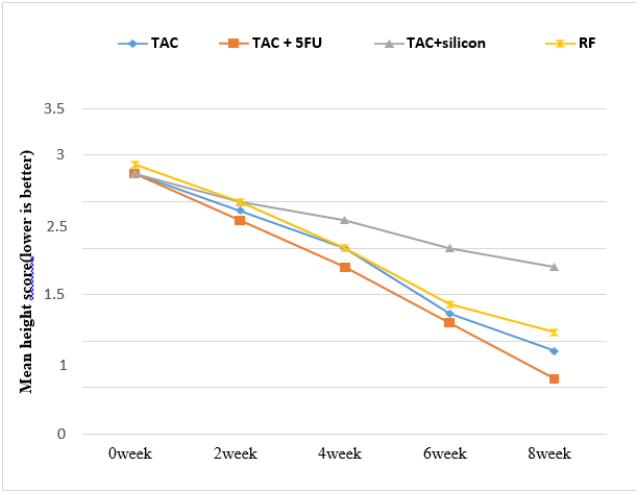

Fig. 4: Rate of change in height to keloid with different modalities

The response of different treatment modalities on height of keloid was best observed in TAC + 5FU group, followed by TAC alone, RF and then least was in TAC + SGS group. (Figure 4)

At the end of 4 weeks, excellent improvement was found highest in 29.6% of TAC+5FU group, 22.2% in TAC alone, 18.5% RF group and 11.1% in TAC+SGS group. Similarly, good improvement was found highest in 25.9% of TAC+5FU group, 22.2% in TAC alone, 22.2% RF group and 11.1% in TAC+SGS group. (Table 2, Figure 5)

At the end of 8 weeks, excellent improvement was found highest in 51.8% of TAC+5FU group, 44.4% in TAC alone, 40.7% RF group and 25.9% in TAC+SGS group. good improvement was found highest in 29.6% of TAC+5FU group, 25.9% in TAC alone, 22.2% RF group and 18.6% in TAC+SGS group. (Table 3, Figure 6)

Table 1: Age distribution in different treatment groups

Age	TAC	TAC+ 5FU	TAC + SG	RF
Mean±SD (years)	29 ± 7	30 ± 8	27 ± 7	31 ± 9
pvalue:0.102				

Table 2: Overall improvement in keloid patients treated with different modalities at end of study period (4^{th} week):

Improvement	TAC	TAC+ 5FU	TAC + silicon	RF	P value
Excellent improvement (>75%)	6(22.2%)	8(29.6%)	3(11.1%)	5(18.5%)	**0.00**
Good improvement (51 – 75%)	6(22.2%)	7(25.9%)	3(11.1%)	6(22.2%)	**0.01**
Moderate improvement (26–50%)	9(33.4%)	9(33.4%)	8(29.6%)	7(25.9%)	**0.02**
Mild improvement (<25%)	6(22.2%)	3(11.1%)	13(48.1%)	9(33.4%)	**0.00**

Table 3: Overall improvement in keloid patients treated with different modalities at end of study period (8^{th} week)

Improvement	TAC	TAC+ 5FU	TAC +silicon	RF	P value
Excellent improvement (>75%)	12(44.4%)	14(51.8%)	7(25.9%)	11(40.7%)	**0.00**
Good improvement (51 – 75%)	7(25.9%)	8(29.6%)	5(18.6%)	6(22.2%)	**0.03**
Moderate improvement (26 – 50%)	5(18.6%)	4(14.8%)	8(29.6%)	5(18.6%)	**0.04**
Mild Improvement (<25%)	3(11.1%)	1(3.7%)	7(25.9%)	5(18.6%)	**0.01**

Table 4: Side effects/complication sin keloid patients treated with different modalities

Side effects/ complications	TAC	TAC+ 5FU	TAC + silicon	RF
Skin atrophy	4(14.8%)	2(7.4%)	3(11.1%)	0
Telangiectasia	4(14.8%)	2(7.4%)	4(14.8%)	0
Hypopigmentation	6(22.2%)	3(11.1%)	3(11.1%)	0
Ulceration and infection	0	3(11.1%)	0	8(29.6%)
Recurrence	5(18.5%)	2(7.4%)	2(7.4%)	3(11.1%)

Skin atrophy, telangiectasia, hypopigmentation and recurrence were observed more TAC group therapies.Whereas, ulceration and infection was more frequent with RF treatment, however few cases were also seen TAC+5FU group.(Table 4)

5. Discussion

Although there are plenty of treatment options, but still there is a frustrating number of treatment failures and recurrences. Despite the fact that intralesional TAC injection has shown 50% to 100% clinical efficacy, the result has not been satisfactory as per the study by Ogawa et al.[2] Study by SadeghiniaA et al showed TAC use is associated with numerous unpleasant effects, including, telangiectasia atrophy, and pigmentary changes.[3]

Initially, Fitzpatrick published his 9-year familiarity with the use of TAC + 5-FU. He had the experience of over 5000 injections to more than 1000 patients. He reported that addition of TAC to 5-FU produced more effective results and reduced the pain. Combination was made by addition of 0.1mL of 10mg/mL TAC to 0.9mL of 50mg/mL 5-FU. Injections were repeated for a mean of 5 to 10 times.[4]

It was observed in a study by Nanda S et al that using combination of TAC+5FU resulted in more than 50% improvement in about 80% patients. In comparison with TAC group, it looks as if TAC+5-FU combination is more effectual and offers a faster response with fewer if not without side effects.[5] The findings of the current study are also in accordance with another study by Gupta S et al and M Apikian et al which proposed that intralesional 5-FU combined with low-dose corticosteroid is an option for the treatment of keloid scars and have fewer undesirable effects compared to intralesional corticosteroids alone.[6,7]

Another study by Kontochristopoulos et al[8] observed 85% of patients with more than 50%improvement, but significant recurrence was seen in 45% and ulceration in 30% cases in 12-month follow-up. In the current study, recurrence was not noted probably due to shorter follow-up duration.

Darougheh et al[9] compared 5-FU + TAC with TAC alone. It observed good to excellent (>50%) improvement

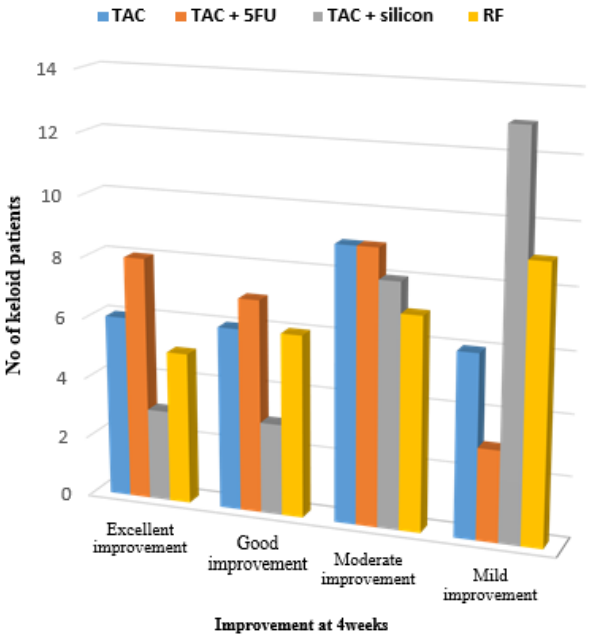

Fig. 5: Overall improvement in keloid patients treated with different modalities tend of study period (4th week):

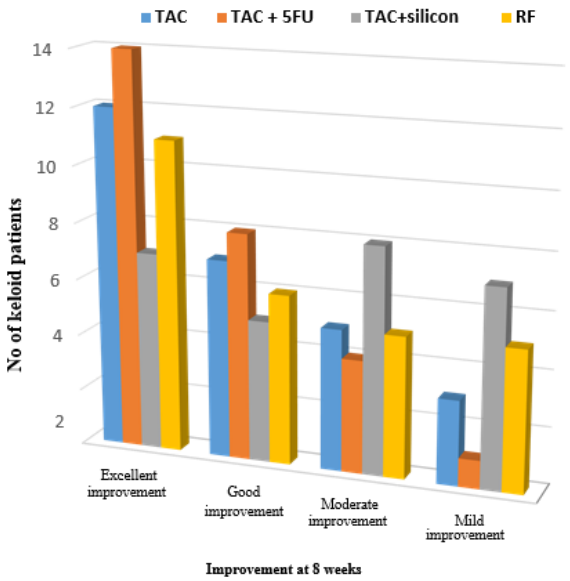

Fig. 6: Overall improvement in keloid patients treated with different modalities at end of study period (8th week):

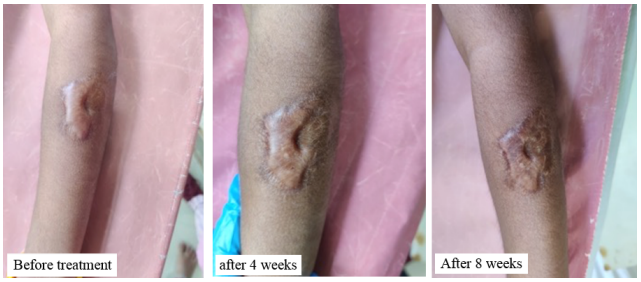

Fig. 7: Patient treated with TAC (group I)

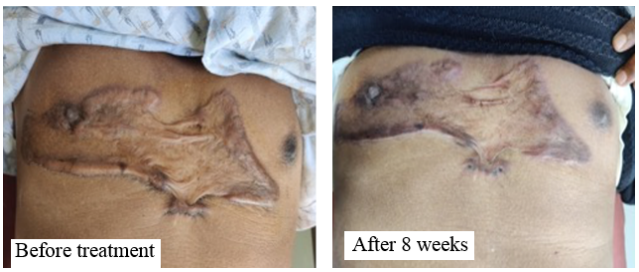

Fig. 8: Patient treated on TAC + 5FU (group II)

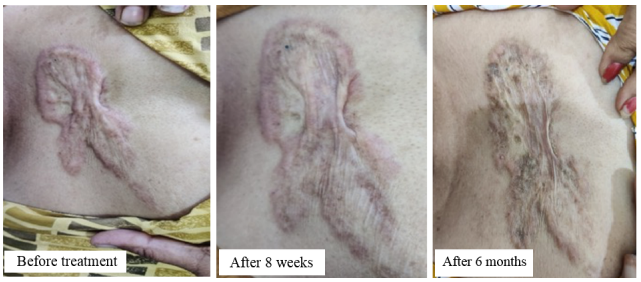

Fig. 9: Patient treated on TAC + SGS (group III)

in 20% of the patients in TAC alone group, and 55% of the patients in the combination group, and on the observer assessment scale good to excellent response was reported in 15% in TAC alone, and 40% in the combination therapy. This 12-week follow-up study showed improvement in all parameters among both groups which are consistent with the current study.

A recent meta-analysis of different RCT's of Darougheh et al, M A Khan et al and Manuskiatti et al[9–11] showed that intralesional 5-FU and TAC has better response in terms of scar height reduction than the TAC alone. A study by Khan et al.[10] showed good to excellent response in 84% of 5-FU + TAC group while 68% response in TAC alone.

In comparison to the previously reported studies, results by Aggarwal[12] using intralesional radiofrequency for keloids were not very exciting. In that study, only 2/17 (11.76%) treated patients showed clearance. Ulceration was seen in 6/17 (35.29%) patients and secondary infection in 2/17 (11.76%) patients. Similar results were obtained in this study too.

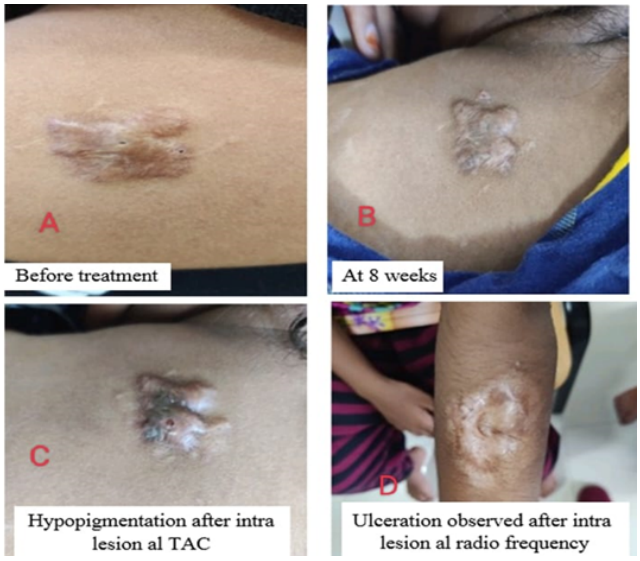

Fig. 10: A, B: Patient treated with intralesional radio frequency(group IV); **C, D:** Complications
C: Ulceration observed after intralesional radiofrequency;
D: Hypopigmentation after intralesional TAC

Tan E et al[13] failed to demonstrate any significant reduction in the size of keloids treated with the silicone gel sheet. In contrast, intralesional injections of triamcinolone acetonide (40 mg/ml) given at intervals of 4 weeks was found to be effective in causing at least a 50% reduction in keloid size in 94% of treated lesions. In addition to size reduction, there was objective and subjective improvement in colour, texture and the relief of pain and pruritus.

We were not able to reproduce the high success rates of silicone gel sheet in treating keloids reported by other authors. However, our results do not address the effectiveness of silicone gel sheet in early keloids.

Gupta el al[1] reviewed existing modalities of treatment and suggested that intralesional injection of 5-FU is considered as a safe and effective treatment, when used either alone or in combination with intralesional injection of corticosteroids for treatment of keloids.

6. Conclusion

Given the aforementioned findings, we believe that the type of response—in terms of the number of procedures required and the flattening of lesions, pliability and overall improvement, was significant in group TAC + 5FU. However, TAC groups had shown some side effects like atrophy, hypopigmentation and recurrence. Ulceration was more commonly seen in RF group, and few cases were also reported in TAC + 5FU group.

TAC + SGS was least effective in treating the keloids in this study.Thus, this study has clearly shown that the combination therapy of 5FU+TAC is more efficacious having fewer undesirable effects compared to TAC alone in the treatment of keloids.

7. Limitation

Patients could not be followed up after completion of the treatment for prolonged periods to assess the rate of recurrence

8. Source of Funding

None.

9. Conflict of Interest

None.

References

1. Gupta S, Sharma VK. Standard guidelines of care: Keloids and hypertrophic scars. *Indian J Dermatol Venereol Leprol*. 2011;77(1):94–100. doi:10.4103/0378-6323.74968.
2. Ogawa R. The most current algorithms for the treatment and prevention of hypertrophic scars and keloids. *Plast Reconst Surg*. 2010;125(2):557–68. doi:10.1097/PRS.0b013e3181c82dd5.
3. Sadeghinia A, Sadeghinia S. Comparison of the efficacy of intralesional triamcinolone acetonide and 5-fluorouracil tattooing for the treatment of keloids. *Dermatol Surg*. 2012;38(1):104–9. doi:10.1111/j.1524-4725.2011.02137.x.
4. Fitzpatrick FE. Treatment of inflamed hypertrophic scars using intralesional 5-FU. *Dermatol Surg*. 1999;25(3):224–32. doi:10.1046/j.1524-4725.1999.08165.x.
5. Nanda S, Reddy BS. Intralesional 5-fluorouracil as a treatment modality of keloids. *Dermatol Surg*. 2004;30(1):54–6. doi:10.1111/j.1524-4725.2004.29382.x.
6. Gupta S, Kalra A. Efficacy and safety of intralesional 5-fluorouracil in the treatment of keloids. *Dermatology*. 2002;204(2):130–2. doi:10.1159/000051830.
7. Apikian M, Goodman G. Intralesional 5-fluorouorouracil in the treatment of keloid scars. *Australas J Dermatol*. 2004;45(2):140–3. doi:10.1111/j.1440-0960.2004.00072.x.
8. Kontochristopoulos G, Stephanki C, Panagiotopoulos A, Stephani K, Argyrakost, Petridis A, et al. Intralesional 5 - Flourouracil in the treatment of keloids; an open clinical and histopathological study. *J Am Acad Dermatol*. 2005;52(3):474–9.
9. Darougheh A, Asilian A, Shariati F. Intralesional triamcinolone alone or in combination with 5-fluorouracil for the treatment of keloid and hypertrophic scars. *Clin Exp Dermatol*. 2009;34(2):219–23. doi:10.1111/j.1365-2230.2007.02631.x.
10. Khan MA, Bashir MM, Khan FA. Intralesional triamcinolone alone and in combination with 5-fluorouracil for the treatment of keloid and hypertrophic scars. *J Pak Med Assoc*. 2014;64(9):1003–7.
11. Manuskiatti W, Fitzpatrick RE. Treatment response of keloidal and hypertrophic sternotomy scars: comparison among intralesional corticosteroid, 5-fluorouracil, and 585-nm flashlamp-pumped pulsed-dye laser treatments. *Arch Dermatol*. 2002;138(9):1149–55. doi:10.1001/archderm.138.9.1149.
12. Aggarwal A, Ravikumar BC, Vinay KN, Raghukumar S, Yashovardhana DP. A comparative study of various modalities in the treatment of keloids. *Int J Dermatol*. 2018;57(10):1192–200.
13. Tan E, Chua S, Lim J. Topical silicone gel sheet versus intralesional injections of triamcinolone acetonide in the treatment of keloids - a patient-controlled comparative clinical trial. *J Dermatol Treat*. 1999;10(4):251–4. doi:10.3109/09546639909056040.

Author biography

Sreelakshmi T S, Resident

Bela B Padhiar, Professor and Head

Cite this article: Sreelakshmi T S, Padhiar BB. A therapeutic evaluation of various modalities of treatment of keloid-A randomized open label study. *IP Indian J Clin Exp Dermatol* 2023;9(2):103-109.