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Original Research Article

Comparative efficacy of intralesional verapamil hydrochloride, triamcinolone acetonide and combination of both drug in hypertrophic scars and keloids at tertiary care center

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ABSTRACT

Background: Keloids and hypertrophic scars are still a therapeutic problem. Despite numerous proposed therapies reported in the literature, the management of keloid and hypertrophic scars is still challenging as there is no universally accepted treatment regimen. Compare the efficacy intralesional verapamil hydrochloride and triamcinolone acetonide separately as well as combination of both drug in treatment of hypertrophic scars and keloids.
Methods: A retrospective study was carried out at the general surgery department (plastic surgery unit) at the JNUIMSRC Jaipur, Rajasthan. Total of 150 patients (60 males and 90 females) between 18 to 60 years of age were enrolled fulfilling the inclusion criteria. They were randomly categorized in to three groups (group A, B and C), based on treatment they received viz. verapamil alone, triamcinolone alone and combination of both drugs respectively. Assessment of the scars were done prior to or on the day of the first injection and at 24 weeks after the end of injection scheme by Vancouver scar scale (VSS). The decreasing values reflected clinical improvement of the scar.
Results: Better improvement observed in all four parameters: height, vascularity, pliability and pigmentation among patients receiving combination of both triamcinolone-verapamil drugs as compare to those patients receiving drugs separately either verapamil or triamcinolone alone. For parameters height, pliability and pigmentation, the improvement was found to be statistically significant ($p<0.05$)
Conclusions: Study highlights that the combined verapamil and triamcinolone therapy scheme causes remarkable scar improvement in keloid and hypertrophic scars in comparison to single drug scheme.

Keywords: Keloid, Hypertrophic scars, Verapamil, Triamcinolone, VSS

INTRODUCTION

Hypertrophic scars and keloids are dermal fibroproliferative disorders unique to humans that occur following trauma, inflammation, surgery, and that sometimes occur spontaneously.[1] They are characterized by excess development of collagen in the dermis and subcutaneous tissues. Unlike scar characteristics of normal wound repair, the exuberant scarring of keloid and hypertrophic scars can result in disfigurement, contractures, pruritus and pain. These cutaneous fibrotic conditions can be caused by minor trauma to the skin, such as ear piercing, abrasion, tattooing and burns.[2]

Keloids and hypertrophic scars are still a therapeutic problem. These scars are mostly disfiguring and are likely to cause severe psychological problems. Besides the psychological aspect, the physical and functional implications of keloids and hypertrophic scars often cause a notable burden for the patient.[3]

First-line management of keloid and hypertrophic scars include silicone sheeting, pressure dressings and corticosteroid injections. Surgical removal poses a high recurrence risk unless combined with one or several of these standard therapies.[4,5]

Despite numerous proposed therapies reported in the literature, the management of keloid and hypertrophic scars is still challenging as there is no universally accepted treatment regimen.[6,7] Currently, there are many approaches for preventing and treating keloids and hypertrophic scars: intralesional therapy, pressure therapy, cryotherapy, radiotherapy, surgical excision, and even combinations of these therapies.[8-10]

The anti-inflammatory and scar-enhancing properties of corticosteroids on hypertrophic scars and keloids have been investigated and documented thoroughly. They are considered a first-line strategy in the treatment of limited keloidal and hypertrophic scars. The most commonly used corticosteroid in this matter is triamcinolone acetonide, and its efficacy and usefulness as well as its limitations are well known.[11,12] Corticosteroids act by suppressing inflammatory cell migration, and inhibition of fibroblast proliferation at high doses.

In contrast to corticosteroids, the efficacy of verapamil (a calcium antagonist) and the combination of verapamil and triamcinolone on hypertrophic scars and keloids is less studied. It has been demonstrated that calcium channel blockers decrease extracellular matrix production in scars. Furthermore, they depolymerize actin filaments to modify fibroblast morphology by a consequent increased secretion of pro-collagenase.[13] Intralesional verapamil hydrochloride has already been successfully applied for the treatment of keloids.[14]

Hence this study was conducted to assess the efficacy of intralesional verapamil hydrochloride, triamcinolone acetonide and combination of both drug in treatment of hypertrophic scars and keloids at a tertiary care center in Jaipur, Rajasthan.

Aim of study

Aim of the study was to assess and compare the efficacy of two treatment options: intralesional verapamil hydrochloride and triamcinolone acetonide separately as well as combination of both drug in treatment of hypertrophic scars and keloids.

METHODS

The present study was a hospital based, retrospective study was carried out at the general surgery department (plastic surgery unit) at the JNUIMSRC Jaipur, Rajasthan from December 2020 to June 2021 after obtaining ethical approval from the institutional ethic committee. A total 150 patients were randomly selected for the study of which 90 were females and 60 were males. Among these selected patients, 80 patients were with keloid scars and 70 were with hypertrophic scars. All enrolled patients were diagnosed with hypertrophic or keloid scarring by a team of experts, consisting of a senior plastic surgeon, a resident plastic surgeon, a junior resident doctor and a physiotherapist specialized in scar therapy. The selected patients were aged between 18 to 60 years who underwent intralesional verapamil hydrochloride or triamcinolone acetonide or a combined therapy of triamcinolone and verapamil injections in order to improve their hypertrophic or keloid scar. While those patients who received an additional scar treatment like Radiotherapy, pressure therapy or silicone at the time study were excluded and patients with loss to follow up.

Patients were then categorized in to three groups (Group A, B and C), based on treatment they received. Group A patients (n=50) received intralesional verapamil hydrochloride, group B patients (n=50) received triamcinolone acetonide and group C patients (n=50) received combination of both drug in treatment of hypertrophic scars and keloids (Table 1)**.**

Group A (n=50): Patients received intralesional verapamil hydrochloride every 3 weeks for a maximum of 8 sessions or until complete flattening of the scar. Each intralesional session was preceded by cryotherapy using cryospray technique for 20 seconds at 1 cm distance from the lesion. The maximum volume of verapamil (2.5 mg/ml) at each session was 1.5 cc.

Group B (n=50): Patients received intralesional triamcinolone acetonide every 3 weeks for a maximum of 8 sessions or until complete flattening of the scar. Each intralesional session was preceded by cryotherapy using cryospray technique for 20 seconds at 1 cm distance from the lesion. The maximum volume of triamcinolone (20 mg/ml) at each session was 1.5 cc.

Group C (n=50): Patients received combination of both drug that consist of a 1:1 mixture of triamcinolone (Kenacort-A, Bristol Myers Squibb, New York, United States 40 mg/ml) and verapamil (2.5 mg/ml). The mean volume of the mixture injected in scars was between 1 and 2 ml. Injection scheme: a first injection (t=0), the second injection a week after the initial injection, and an additional third injection 3 weeks after the first injection.

In total, 150 eligible patients completely followed the proposed injection scheme as they form baseline in all the three treatment categories. Patients were followed up at 24 weeks at the end of the injection scheme in each treatment categories.

Assessment of the scars were done prior to or on the day of 1st injection and at 24 weeks after end of injection scheme by VSS.[15] The mentioned scale scores the scars on 4 parameters: height, vascularity, pliability, and pigmentation. Scar height was accurately measured with a ruler in mm. Scar vascularity and pigmentation were

assessed by visual inspection. Scar pliability was subjectively assessed by palpation. For study parameters in each group, mean value and SD were calculated. The decreasing values reflect clinical improvement of scar.

Statistical analysis

Data was coded and entered in MS excel 10.0 and analyzed using SPSS trial version 22.0. As study was planned to evaluate efficacy of triamcinolone, verapamil and combination of both drug with respect to scar outcome, so scar scores at baseline and follow-up visit are presented as means with standard deviations. The Wilcoxon test was used to test significant improvement of VSS parameters in each group. Appropriate tables and figures are generated. P<0.05 was considered statistically significant at 5% level of significance.

RESULTS

The present study included 150 patients diagnosed with hypertrophic or keloid scarring aged 18-60 years with a mean age of 34.36±9.21 years. Table 1 shows categories of patients based on treatment they received.

Table 1: Characteristic of the patients, (n=150).

Characteristics	Variables	N	Percent (%)
Gender	Male	60	40
	Female	90	60
Group based on treatment received	Group A: Verapamil	50	33.3
	Group B: Triamcinolone	50	33.3
	Group C: Combination of both drugs	50	33.3

Equal no. of patients received intralesional verapamil hydrochloride (n=50), triamcinolone acetonide (n=50), combination of both drug in treatment of hypertrophic scars and keloids. Scar location shown in Table 2.

Table 2: Distribution of scar location, (n=150).

Scar locations	Frequency	Percent (%)
Extremities	22	14.7
Face/head/neck	47	31.3
Pre-sternal	12	8.0
Shoulder	13	8.7
Sternum	31	20.7
Thorax	9	6.0
Abdomen	8	5.3
Back	8	5.3

The means and SD for baseline and 24 weeks follow-up for all 4 VSS parameters: height, vascularity, pliability, pigmentation in verapamil, triamcinolone and combination treatment groups were assessed.

For height parameter, in all 3 study groups, there was a reduction in height at 24 weeks follow-up time. Remarkably more reduction observed among patients receiving combination treatment (0.19±0.21 at 24 weeks vs 4.17±1.56 at baseline) as compared to patients receiving drugs separately either verapamil (3.26±1.69 at 24 weeks vs 4.16±1.72 at baseline) or triamcinolone (0.86±0.61 at 24 weeks vs 4.19±1.88 at baseline) alone (Figure 1). P among all 3 groups was statistically significant (p<0.05) while comparing at baseline and follow up.

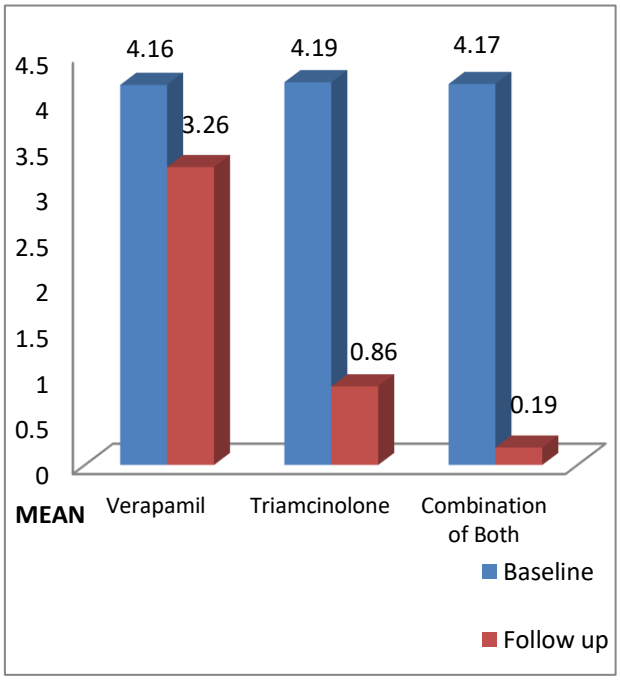

Figure 1: Mean VSS score: height at baseline and follow up.

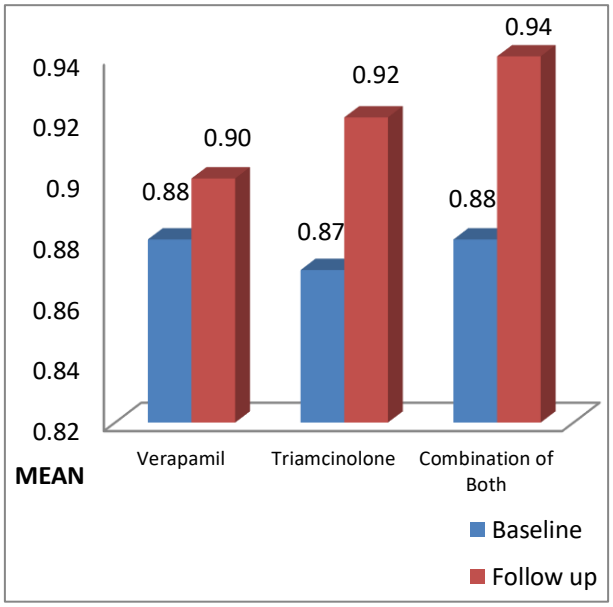

Figure 2: Mean VSS score: vascularity at baseline and follow up.

Figure 2 illustrates that among patients received combination of both drug in treatment, there was more improvement in the vascularity (0.94±0.76 at 24 weeks vs 0.88±0.74 at baseline) as compared to patients receiving drugs separately either verapamil (0.90±0.64 at 24 weeks vs 0.88±0.79 at baseline) or triamcinolone (0.92±0.69 at 24 weeks vs 0.87±0.95at baseline) alone. P value among the all three groups was statistically not significant (p value >0.05) while comparing at the baseline and follow up.

Better improvement in pliability was observed in the group receiving combination of triamcinolone-verapamil compared with the groups receiving drugs separately either verapamil or triamcinolone alone as shown in Figure 3. P value among all three groups was statistically significant (p<0.05) while comparing at baseline and follow up.

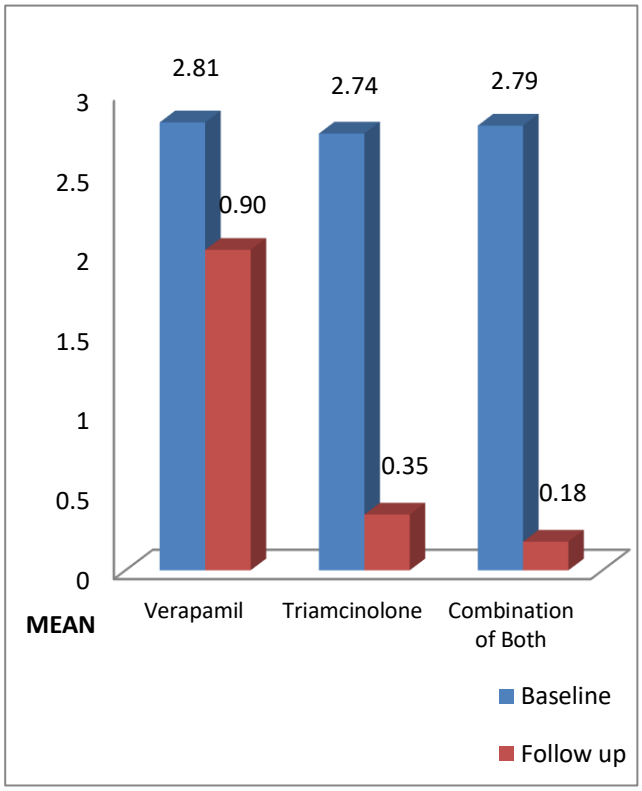

Figure 3: Mean VSS score: pliability at baseline and follow up.

It was observed that p value among group receiving verapamil was statistically not significant (p value >0.05) for pigmentation while comparing at baseline and follow up. Significant improvement in the pigmentation (p value <0.05) was observed in the group receiving combination of triamcinolone-verapamil drugs and also in the group receiving triamcinolone alone, however there was more reduction in pigmentation among group receiving combination drugs (0.12±0.10 at 24 weeks vs 0.38±0.41 at baseline) as compared to triamcinolone alone (0.16±0.12 at 24 weeks vs 0.40±0.88 at baseline) as illustrated in Figure 4.

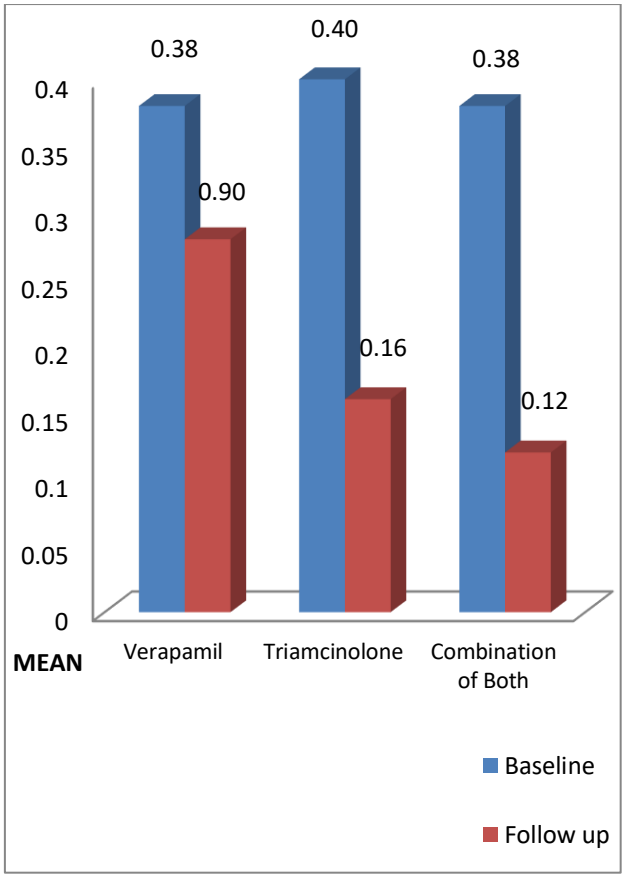

Figure 4: Mean VSS score: pigmentation at baseline and follow up.

DISCUSSION

A hospital based retrospective study was carried out at the plastic surgery unit of general surgery department at the JNUIMSRC Jaipur, Rajasthan to assess and compare the efficacy of two treatment options: intralesional verapamil hydrochloride and triamcinolone acetonide separately as well as combination of both drug in treatment of hypertrophic scars and keloid. A total of 150 patients were followed up from baseline to 24 weeks to evaluate hypertrophic and keloid scarring by VSS having 4 parameters: height, vascularity, pliability, and pigmentation.

We found better improvement observed in all four parameters: height, vascularity, pliability, and pigmentation among patients receiving combination of both triamcinolone-verapamil drugs as compare to those patients receiving drugs separately either verapamil or triamcinolone alone.

This study suggests that the combined verapamil and triamcinolone therapy scheme causes remarkable scar improvement in keloid and hypertrophic scars in an early stage (24 weeks) in comparison to single drug scheme (Figure 5).

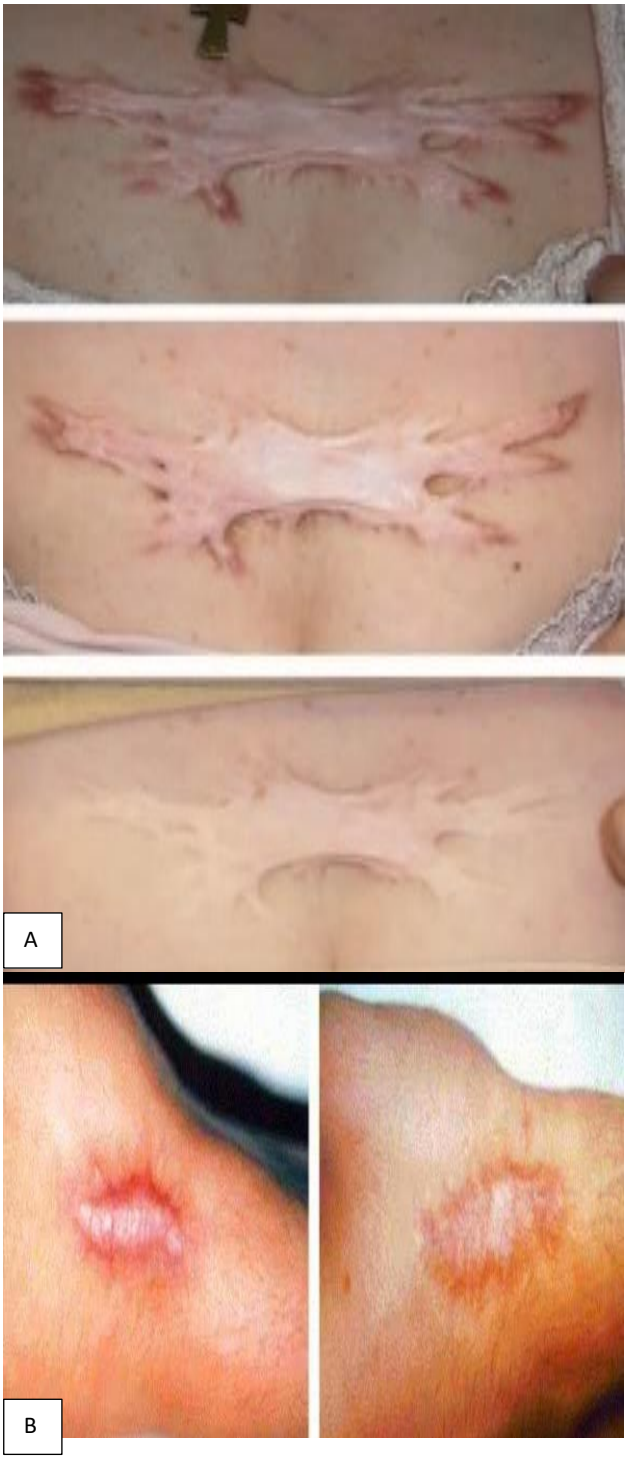

Figure 5 (A and B): Scar improvement in keloid and hypertrophic scars in an early stage (24 weeks).

There have been similar researches in accordance to the present study. Kant et al revealed a fast and abiding improvement of both keloid and hypertrophic scars after treatment with the combination therapy in their study conducted at the department of plastic surgery at the Maastricht University hospital among 58 patients.[16] In another study, Saki et al conducted a randomized, single-blind, single-group comparison with 15 patients (30 scars) to compare the effects of intralesional triamcinolone with verapamil injections.[17] In both study groups there was a reduction in height and pliability at the end of the study. Better improvement in height and pliability was seen with triamcinolone in comparison with verapamil. Also, Shanthi et al caried out a randomized, single blind, parallel group study in which 54 patients were allocated to receive either verapamil or triamcinolone.[18] There was a reduction in vascularity, pliability, height and width of the scar with both the drugs after 3 weeks of treatment. These changes were present at one year of follow-up after stopping treatment. Scar pigmentation was not changed desirably by either drug. Length of the scars was also not altered significantly by either drug. The rate of reduction in vascularity, pliability, height and width of the scar with triamcinolone was faster than with verapamil.

Multiple studies have proven the effect of triamcinolone and verapamil separately, whereas triamcinolone still is considered being a gold standard in non-surgical management for hypertrophic scarring and keloids. Nevertheless, verapamil has shown to be a promising extra modality in treatment of keloid and hypertrophic scar and it may even function as a suitable alternative to triamcinolone in the treatment of hypertrophic scars and keloids.[19,20]

A randomized parallel group study concluded that both triamcinolone and verapamil could achieve scar flattening in hypertrophic scars and keloids, yet it needed to be clinically investigated if both drugs could be combined in a single injection to derive a synergistic and enhanced response.[13] Furthermore, combination therapy of triamcinolone and verapamil exerted an efficacy equivalent or even better than double-dose verapamil alone in the treatment of hypertrophic burn scars in mice.[21]

The results of the present study suggests that for a safer treatment for patients with keloids, verapamil could be considered however it is not as effective as triamcinolone. And the combination of both drugs is the most effective therapy.

CONCLUSION

It can be concluded that combination therapy of triamcinolone and verapamil results in better scar improvement as compared to drugs given separately either verapamil or triamcinolone alone. Further research using well-controlled double-blind clinical trials with larger study participants and multi centric involvement with the presence of a control group would be recommended for further clinical appraisal of the efficacy of combination therapy of triamcinolone and verapamil drugs.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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