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EFFICACY OF INTRALESIONAL VARAPAMIL WITH TRIAMCINOLONE IN THE TREATMENT OF EAR KELOIDS IN SOUTH INDIAN POPULATION : A PROSPECTIVE STUDY .

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ABSTRACT

Background: Keloids are benign fibroproliferative disorders characterized by excessive collagen deposition extending beyond the original wound margins. Intralesional triamcinolone acetonide (TAC) is considered first-line therapy; however, recurrence and adverse effects remain concerns. Verapamil, a calcium channel blocker, has shown promise in modulating fibroblast activity with fewer side effects.

Objective: To evaluate the efficacy and safety of intralesional verapamil combined with triamcinolone acetonide in the management of ear keloids in a South Indian population.

Methods: This prospective study included 30 patients with ear keloids treated at a tertiary care center from Dec2017- Dec2019. Patients received intralesional verapamil (2.5 mg/mL) combined with triamcinolone acetonide (40 mg/mL) in a 9:1 ratio at 0.1 mL/cm of lesion every three weeks for six sessions. Clinical outcomes were assessed using the Vancouver Scar Scale (VSS) at baseline and during follow-up. Statistical analysis was performed using SPSS v21.0, with Wilcoxon signed-rank test applied. A p-value <0.05 was considered significant.

Results: The mean age was 31 years. All patients were female. Bilateral involvement was observed in 53%. The most common symptom was hyperpigmentation (66.6%), followed by itching (40%). Mean VSS score significantly decreased from 7.68 ± 1.89 at baseline to 4.28 ± 2.21 at 18 weeks ($p < 0.05$), representing a 46.2% improvement. Recurrence was observed in 26% during follow-up (13% at 6 months; 13% at 1 year). Pain was universal post-injection, and ulceration occurred in 27%.

Conclusion: Intralesional verapamil combined with triamcinolone acetonide is an effective and relatively safe treatment modality for ear keloids, demonstrating significant reduction in VSS scores with acceptable recurrence rates. Combination therapy may serve as a first-line approach in selected patients.

Keywords: Keloid, Verapamil, Triamcinolone Acetonide, Intralesional Therapy, Vancouver Scar Scale, Combination Therapy

INTRODUCTION

Keloids are scars that extend beyond the wound margins. They have a racial predisposition of 4.5-16% in dark skinned individual. They are multifactorial with a genetic predisposition showing

autosomal dominant trait. Multiple treatment regimes have been demonstrated in case of keloids like surgery, intralesional triamcinolone, Varapamil, 5 fluorouracil, cryotherapy, LASER etc.
Intralesional triamcinolone acetonide (TAC) is considered to be the first line of treatment, however it is effective only against younger keloids, response rate varies from 50% to 100%, and a recurrence rate of 9% to 50% is reported.8 Local side effects due to TAC include dermal atrophy, telengiectasia and pain at the site of injection.
Verapamil, a calcium channel blocker, and an antiarrhythmic agent, has emerged as a useful treatment modality in treatment of keloids.9 It is reported to decrease IL-6 and vascular endothelial growth factor in the central keloid fibroblasts, reducing cell proliferation, increasing apoptosis and expression of decorin, thus inhibiting fibroblast proliferation and migration and reducing keloid.10
It is reported that VPL has lesser side effects as compared to TAC, is cheaper ,by assessing clinical improvement using Vancouver scar scale
My study aims to define the efficacy of intralesional Varapamil +TAC with or without excision combination in management of keloid.

MATERIALS & METHODS

This is a prospective clinical study including all patients presenting with ear keloids attending to ENT OPD of Dr. B. R. Ambedkar medical college for a period of 1 year. After a thorough clinical history & examination, patient will be subjected to complete blood count, liver function tests and renal function tests.
Injection verapamil (VPL) 2.5 mg/ml + TAC(40mg/ml) in the ration of 9:1 at the rate of 0.1ml/cm of lesion was administered intralesionally at an interval of 3 weeks, for a total of 6 sittings, over a period of 18 weeks (4.5 months). Injection Verapamil needs no dilution as it is available in the required concentration of 2.5 mg/ml (vial: 5 mg/2 ml). The lesion was infiltrated with the drug solution, until complete and uniform blanching of the lesion was achieved, using a disposable insulin syringe, and 26 gauge needle. No sedation/analgesia was used prior to the injection. The details of the subject were recorded in a predesigned “case record form” which included the Fitzpatrick skin type, duration, site, number and various other parameters of the keloid. Height, pliability, vascularity, pigmentation and size of the keloid were assessed on VSS. VSS was assessed before treatment with Injection VPL
Any side effects experienced by the patients at the time of injection or after the injection will be noted. The dose will be repeated at weekly intervals for a month and then monthly for 2 months. Follow up of the scar will be done at 4, 8 weeks and 3 & 6 months post treatment& graded by Vancouver scar scale.
Vancouver scar scale
Inclusion criteria:

1. >15 years of age
2. Keloids of the ear

Exclusion critera:

1. Patient who had any treatment for the keloid in the last 6 months,
2. Altered LFT
3. Abnormal RFT
4. WBC counts< 4000 or > 11000
5. Pregnancy or lactating mother

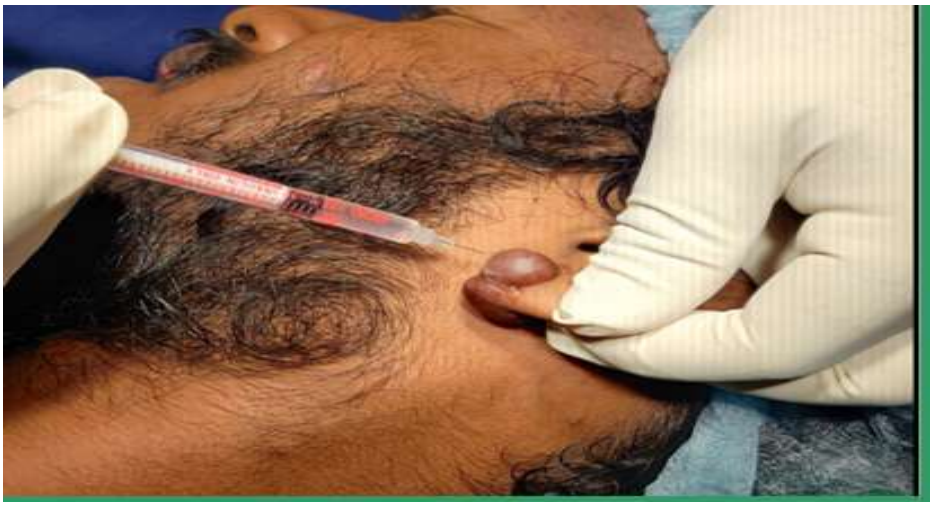

Figure 1:Technique of injecting theVarapamil.

Pigmentation 0-2	Normal Hypopigmentaion hyperpigmentation
Vascularity 0-3	Normal Pink Red Purple
Pliability 0-5	Normal Supple Yielding Firm Banding Contracture
Height 0-3	Normal 0-2mm 2-5mm >5mm

Statistical Analysis

Data analyzed using SPSS version 21.0. Wilcoxon signed-rank test applied. $p < 0.05$ considered statistically significant.

RESULTS

Demographics

- Mean age: 31 years
- All patients female
- Bilateral keloids: 53%
- History of ear piercing: 100%
- Previous treatment: 80%

Clinical Characteristics

- Largest lesion: 2 × 1 cm
- Smallest lesion: 0.25 × 0.25 cm
- Hyperpigmentation: 66.6%

- Itching: 40%
- Pain: 13%

Vancouver Scar Scale Outcomes

- Baseline mean VSS: 7.68 ± 1.89
- Post-treatment mean VSS: 4.28 ± 2.21
- Mean reduction: 3.40 ± 1.44 (46.21%)
- Statistical significance: $p < 0.05$

Recurrence

- No recurrence: 74%
- Recurrence at 6 months: 13%
- Recurrence at 1 year: 13%

Adverse Effects

- Pain: 100%
- Ulceration: 27%
- No systemic adverse effects repo
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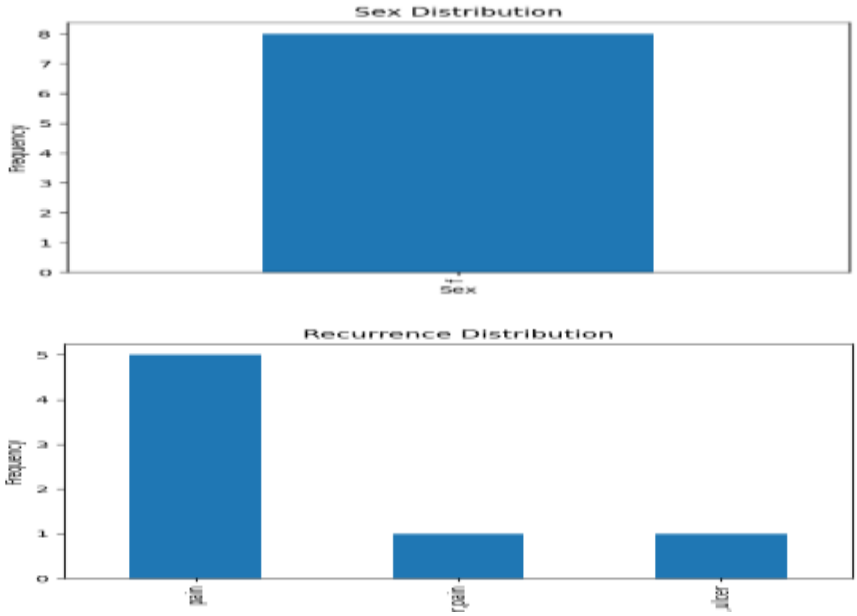


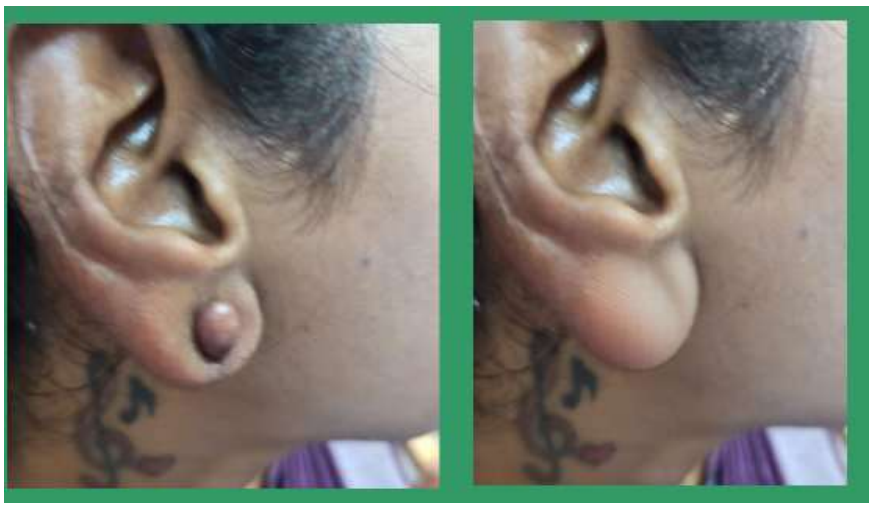
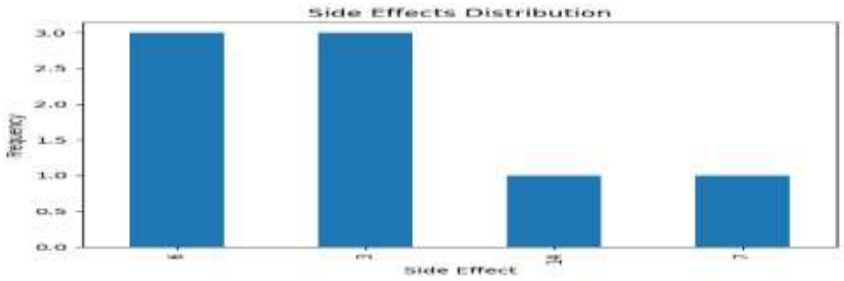


Figure2: Before and After the treatment(Varapamil + Triamicilone+ Surgery)



The mean age group of the study population was 31 years. All the subjects were female. Amongst the 30 patients in this study, 16 were bilateral, 8 were left sided & 6 were right sided. Duration of the keloids had a median of 6 months on the right & 1 year on the left, varying from 3 months to 8 years. All the study samples attributed cause of keloids to trauma to ear mostly ear piercing. Symptomatology varied from hyperpigmentation in 66.6% followed by itching in 40% & pain in 13%. (fig 1)History of previous treatment including surgery, intralesional steroid injections were noted in 80% of the population. The largest of keloids measured 2 x 1 cm, smallest being 0.25 x 0.25 cm. The dosage of verapamil used was in the range of 2.5 mg/ml, dose of TAC was 1.6-4mg/ml. Most common side effects of the injections noted were pain & ulcer in the wound. 100 % samples had pain post injections, 27 % had ulcers. Patients were followed up for maximum of 1.9 years & minimum of 1 year. 74% had no recurrence, 13 % had a recurrence after 6 months, another 13 % had recurrence after 1 year(fig 2).Statistical analysis Data was analyzed using Statistical Package for Social Sciences (SPSS), version 21.0. Wilcoxon signed rank was used to assess the outcome. A „p" value less than 0.05, indicated a statistically significant change. RESULTS A total of 30 patients of keloid, were treated with intralesional injection verapamil 2.5 mg/ml. All 30 patients completed the study. Male patients were 14 (56%) and female 11 (44%). Age of the patients varied from 12 years to 49 years, mean age was 30.72 (±11.23) years (Table 1). Family history of Keloid was present in 3 (12.0%) patients. The majority (64.0%) had Fitzpatrick skin type IV. Duration of Keloids ranged from 1 to 36 months with a median duration of 8 months (Table 1). The majority (92%) had one or two keloids; none of the patient had more than three keloids (Table 2). The majority (92%) of keloids were either on the chest or shoulders (Table 3). Table 1: Demographic data. Demographic characteistics Male 14 (56%), Female 11 (44%) Gender Ratio M:F- 1.27:1 Age in years 12-49 Family history +ve 3 (12.0%) Mean 30.72±11.23 yrs -ve 22 (88%) Fitzpatrick skin type Type IV (64.0%) Duration 1 to 36 months Type V skin (36.0%) Median- 8 months Table 2: Number of keloids. Patients Number of Keloids 15 (60%) One 8 (32%) Two 2 (8%) Three An assessment of VSS score was done at baseline and at 3 weeks, after the last injection, i.e. at 18 weeks from the first injection. At baseline, mean VSS score was 7.68±1.89 (median 8), which reduced to 4.28±2.2

The term keloid was originally described in 1800s as "cheloid," derived from the Greek word "chele" means "crab claw." By definition and in distinction from a hypertrophic scar, keloids extend beyond the borders of the original wound and invading into/around normal skin. Usually appear as firm nodules, often pruritic and painful, and generally do not regress spontaneously.Cell and biochemical events in wound repair can be divided into the following stages: inflammatory reaction, cell proliferation and synthesis of the elements which make up the extracellular matrix, and the posterior period, called remodelling. Keloid is characterized by abnormal collagen deposition, increased fibroblasts & production of TNF-alpha, INF-beta & IL-6 resultling in increased fibrosis. There are multiple treatments proposed for keloids. A review study of keloids [1] implied that multiple management of keloids were in vogue including excision, intralesional TAC, LASER, cryotherapy, radiotherapy, pressure therapy and therapy with immunosuppressive agents . They concluded that combination therapy is better than monotherapy in treatment of keloids.(median 5) at final follow up, showing a mean change of 3.40±1.44 (46.21%). On evaluating the data statistically, it was found to be significant p value.

DISCUSSION

Keloids pose significant cosmetic and psychological morbidity. While intralesional corticosteroids remain standard therapy, adverse effects and recurrence remain problematic.Verapamil inhibits extracellular matrix production and promotes collagen degradation, offering a mechanistic advantage. The present study demonstrated a statistically significant reduction in VSS scores, indicating meaningful clinical improvement.The recurrence rate (26%) compares favorably with literature reporting recurrence rates up to 50% with steroid monotherapy. Although pain was universal, no long-term complications such as dermal atrophy or hypopigmentation were observed.Combination therapy appears superior to monotherapy, aligning with previous literature supporting multimodal approaches.

Limitations include small sample size and single-center design.

Keloids cause cosmetic disfigurement, functional impairment and a significant morbidity.6,7 A variety of treatment such as pressure therapy, silicone gel sheeting, intralesional bleomycin or interferon or corticosteroid injections, cryotherapy, surgical manipulation, laser and radiotherapy are being used. No particular treatment is suitable or effective in all the cases of keloid.17 Intralesional corticosteroids seem to be more effective, however they cause local adverse effects such as hypopigmentation, dermal atrophy and menstrual irregularities. Among the emerging therapies, verapamil (VPL) is reported to be effective, relatively safer and much cheaper than TAC.9 Verapamil inhibits the synthesis and secretion of extracellular matrix molecules, including collagen, glycosaminoglycans, fibronectin and increases collagenase by inducing procollagenase expression.18 This study was done to evaluate efficacy of VPL in treatment of the keloid, in skin phototype IV and V. The drug VPL was used in the concentration of 2.5 mg/ml intralesionally, and VSS was used for assessment of the improvement.19-21 The actual amount of dose of the drug being injected, with respect to area and thickness of the keloid, cannot be measured as thickness of the keloid varies from lesion to lesion, and also within the lesion. Consequently in this study, complete blanching of the keloid at the time of intralesional injection, was considered to be the end point of the dose

CONCLUSION

Ear keloids are cosmetically challenging for a patient. There are multiple management techniques for a keloid but none has proved to be a 100 % effective or expensive like LASER, Radiotherapy etc. Intralesional verapamil gives very good to excellent improvement in a large number of patients. The drug is available as a thin solution, and is easy to inject, using a fine gauge needle. It does not cause adverse effects such as local dermal atrophy or hypopigmentation, and is relatively safe. Pain following verapamil is severe and analgesics may be required. In this study, good results were noted with intralesional injection of keloid with Varapamil &TAC post surgical excision of the same. Hence Varapamil with TAC should be used as first line of management of keloids in the background of normal blood parameters

Intralesional verapamil combined with triamcinolone acetonide is an effective, safe, and cost-effective modality for the treatment of ear keloids. It significantly reduces scar parameters with acceptable recurrence rates and minimal serious adverse effects. Combination therapy should be considered as a first-line treatment in selected patients

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