"AN INTERVENTIONAL STUDY COMPARING INTRALESIONAL VERAPAMIL AND INTRALESIONAL TRIAMCINOLONE ACETONIDE IN THE TREATMENT OF KELOIDS IN A TERTIARY CARE HOSPITAL"

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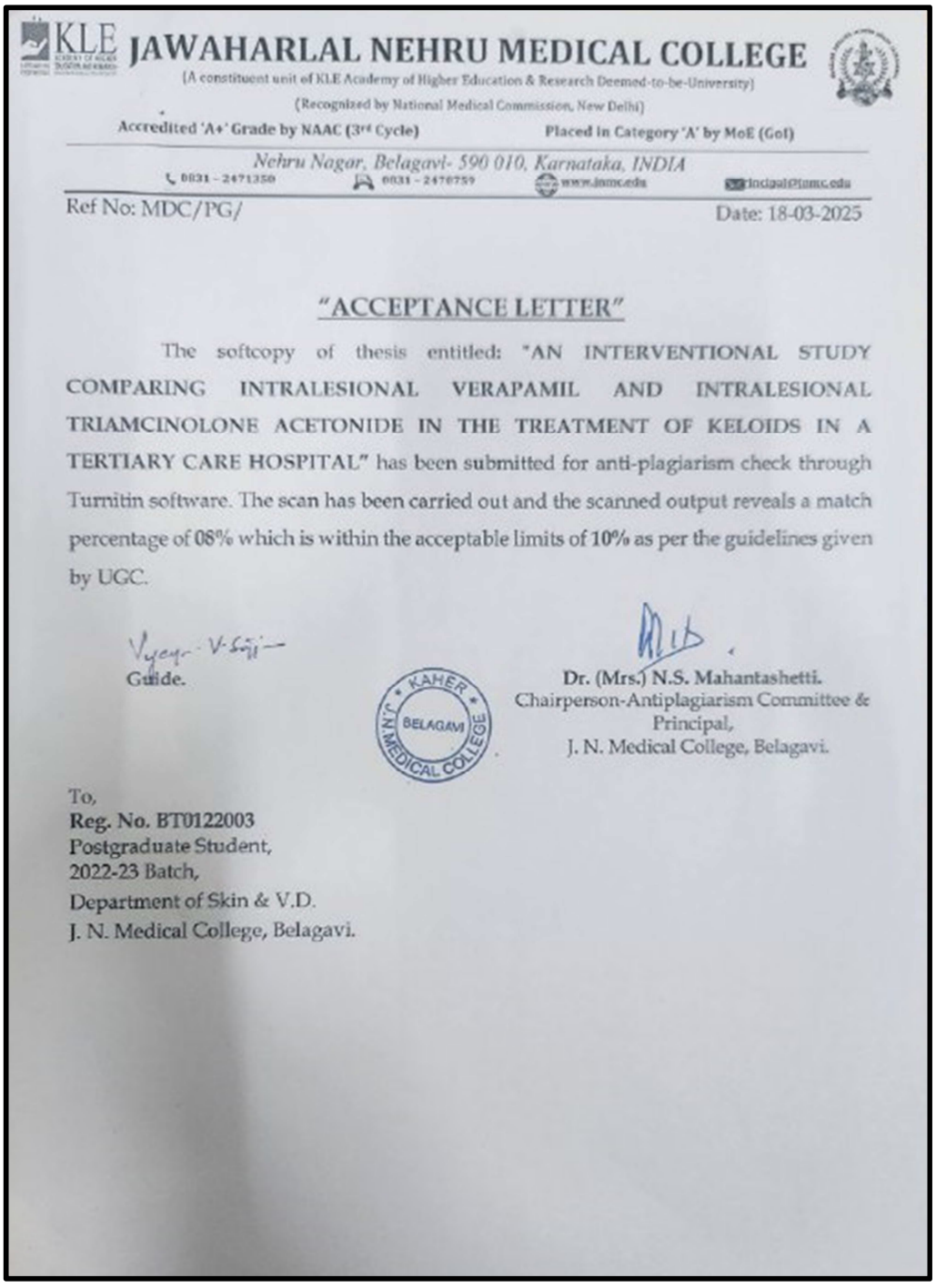

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ABSTRACT

- **Background:** Keloids is caused by abnormal hyperproliferation of dermal fibroblast, causing expansion beyond boundaries of insult. Intralesional (IL) triamcinolone acetonide (TAC) causes inhibition of fibroblast. Intralesional verapamil, a calcium channel blocker activates procollagenase causing depolymerization of actin, inhibiting incorporation of proline and slowing action potential by which it reduces pain and pruritis associated with keloids. This study compares both the modalities for treatment of keloids.
- **Aims and Objectives:** To assess and compare the efficacy, safety, reduction in pain and pruritis and side effects between intralesional verapamil hydrochloride and triamcinolone acetonide in treatment of keloid in patient aged 18 to 70 years.
- **Materials and Methods:** It is open label, non-randomized, interventional study of 33 patients with two keloids. First keloid received intralesional triamcinolone acetonide 40 mg/ml and second keloid intralesional verapamil hydrochloride 2.5 mg/ml, given every 3 weeks for 6 weeks (three sessions). Assessment done by Vancouver scar scale (VSS), volume, visual analogue scale, pain score while injecting, pruritis score and side effects at 9 weeks.
- **Results:** There was significant difference among the height and volume parameters of VSS scale in triamcinolone group as compared to the verapamil group (p value <= 0.05). There was no significant difference seen in vascularity, pigmentation, pliability and pruritis score between both the groups. There was significant difference in the visual analogue scale and pain score associated with keloids in triamcinolone group as compared to verapamil group. There was also significant difference seen in the pain score while injecting, with verapamil having more pain while injecting.

- **Keywords:** Triamcinolone acetonide, Verapamil hydrochloride, Vancouver scar scale, keloids
- **Conclusion:** Both the groups showed improvement in pigmentation, vascularity, pliability and pruritis. Significant improvement in height, volume, visual analogue scale in triamcinolone group. Side effects like telangiectasia, atrophy and hypopigmentation, seen in the triamcinolone group were not observed in verapamil group and more effective in keloids associated with vascularity compared to triamcinolone except having a higher pain score while injecting. Both groups were effective in reducing the pain and pruritis associated with keloid.
- **Limitations:** Sample size was only less. (n=33)

LIST OF ABBREVIATIONS

ABBREVIATIONS	EXPANSIONS
IL	INTRALESIONAL
TAC	TRIAMCINOLONE ACETONIDE
DM	DIABETES MELLITUS
CREBBP	CYCLIC-AMP-REGULATED ENHANCER BINDING PROTEIN
OCRL	OCULOCEREBRORENAL SYNDROME OF LOWE
FLNA	FILAMIN-A
TAC	TRIAMCINOLONE ACETONIDE
IL-6	INTERLEUKIN-6
VEGF	VASCULAR ENDOTHELIAL GROWTH FACTOR
SNARE	SOLUBLE N-ETHYLMALEIMIDE-SENSITIVE FACTOR ATTACHMENT PROTEIN RECEPTOR
IGF-1	INSULIN LIKE GROWTH FACTOR ONE

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INTRODUCTION

Keloids are caused by excessive proliferation of fibrous tissue and abnormal wound healing that can result after any kind of inflammation or trauma. The earliest description of keloids, as abnormal scar formations, was recorded by Egyptian surgeons, in the Smith papyrus which contains details about surgical techniques that dates around 1700 BC.[1] The word "keloid" means "crab claw" was introduced in 1806 by Alibert and was used to describe how they spread from the scared tissue and extends laterally into healthy tissue. [1]

Keloids result from hyperproliferation of fibroblast which are generally hyperactive and there in turn production of excessive growth factors resulting in the proliferation and it's spread beyond the boundaries of insult.

Various factors have been listed in the pathogenesis of keloid formation like trauma, genetic factors including various syndromes that have increased risk of developing keloids and environmental factor triggering keloids at specific sites of body owing to the specific pressure induced resulting in their particular shapes[2] There are various theories of keloid formation that have been mentioned below.

Keloids can be also differentiated from hypertrophic scar based on its clinical features and histopathology. There is also difference between them at cellular level and racial differences have also been found out.

Multiple treatment options are available for management of keloids such as different intralesional therapy, topical therapy, cryotherapy and laser therapy. Newer modalities for its treatment are still being developed acting by various mechanism like decreasing the proliferation of fibroblast and various growth factors involved in its pathogenesis and reducing the inflammation.

AIMS AND OBJECTIVES

Primary objective: To assess and compare the efficacy of: intralesional verapamil hydrochloride and triamcinolone acetonide in treatment of keloid in patient aged 18 to 70 years.

Secondary objective: To assess and compare the safety of: intralesional verapamil hydrochloride and triamcinolone acetonide in treatment of keloid in patient aged 18 to 70 years.

REVIEW OF LITERATURE

KELOID: Keloids form due to the excessive growth of fibrous tissue after a cutaneous injury. They are dermal fibroproliferative growths without any malignant potential. [1]

HISTORY: The earliest description of keloids, as abnormal scar formations, was recorded by Egyptian surgeons, in the Smith papyrus which contains details about surgical techniques that dates around 1700 BC.[1]The word "keloid" means "crab claw" was introduced in 1806 by Alibert and was used to describe how they spread from the scared tissue and extends laterally into healthy tissue. [1]

EPIDEMIOLOGY: Individuals who are having darker skin tones like Africans and Assians have increased rates of developing keloids as compared to Caucasians, with incidence rates being 5-10% in Africans, 0-0.1% in Asians and less than 0.1% in other countries. The likelihood of developing keloids is particularly elevated during pregnancy and puberty. Those having a positive family history also have increased risk but particular gene for keloids has not been identified yet.[2,3]

ETIOLOGY

1. **GENETIC FACTORS:** Keloid formation is associated with genetic polymorphism and mutations like those involving TGF-beta1 genes, etc.[4] Keloids have a familial tendency. There are well-known genetic conditions associated with keloids and have HLA associations such as HLA-DRB115, HLA-DQB1 and HLA-DQA1 and these genetic diseases can decrease or increase the formation of keloid. Pachydermoperiostitis also have increased risk of developing keloids. The diseases mentioned below have an increased risk of keloid formation in body:

1. RSTS-Rubinstein-Taybi syndrome.
2. Ehlers-Danlos syndrome.
3. Lowe syndrome.
4. Novel X-linked syndrome
5. Dubowitz syndrome.
6. Noonan syndrome.
7. Goeminne syndrome.
8. Pachydermoperiostitis.

❖ **RUBINSTEIN-TAYBI SYNDROME(RSTS)-**

1. Genetic defect- Involves mutations present in the gene that encodes for

   a) *CREBBP located* in chromosome 16p13.3

   b) E1A binding protein (Ep300) located in chromosome 22.

2. Clinical features:

- Facial abnormalities like nose is beaked, eyebrows are arched, arched palate, columella extends below the nasal alae, atypical smile referred to as grimacing and mild micrognathia.
- Hand abnormalities- Enlarged thumb and clinodactyly of fifth finger[(5)]

3. Keloid formation tendency being 24%.

❖ **EHLERS DANLOS SYNDROME TYPE FOUR (VASCULAR TYPE)-**

1. Genetic defect: Gene-COL3A1 which encodes pro alpha-1 chain of type three collagen.
2. Clinical features: Increased tendency to have bruises, shiny skin and increased risk of uterine and gastro intestinal and vascular complications.
3. Extensive keloid formation [(2)]

- **LOWE SYNDROME/OCRL-**

1. Genetic defect: OCRL-1 protein is reduced because of mutation of OCRL gene.
2. Clinical features: It affects the renal system particularly kidneys, eyes and nerves.
3. Keloids are present over cornea.[2]

- **NOVEL X-LINKED SYNDROME-**

1. Genetic defect: Mutation in FLNA gene causes it. [2]
2. Clinical features: Cardiac valvular disease and reduced joint mobility.
3. Keloid formation occurs spontaneously.

- **DUBOWITZ SYNDROME-**

1. Genetic defects: Autosomal recessive transmission.
2. Clinical features: Restriction in intrauterine growth, having a short stature, different facial characters, atopic dermatitis and mental retardation are a part of this syndrome.[6]
3. Spontaneous keloidal lesions.

- **NOONAN SYNDROME**

1. Genetic defect: Multiple genes involved like BRAF, RAS etc. Have an Autosomal dominant type of inheritance.
2. Clinical features: They have features like low set ears and dropping of eyelids and broad cranial features, abnormalities in bone, congenital defects in cardiac system, growth retardation and psychomotor abnormalities.
3. Keloidal tissue formation.[2]

❖ **GOEMINNE SYNDROME**

1. Genetic defect: exact gene not identified, X-linked genetic mutation.
2. Clinical features: Renal dysplasia, cryptorchidism and congenital muscular torticollis.
3. Multiple spontaneous keloid formation risk.(2)

2. ENVIRONMENTAL FACTORS

Environmental triggers play a significant role in the progression and also in development of keloids. Most commonly occurring sites of body where keloids occur are:

1. Anterior chest.
2. Scapula.
3. Neck.
4. Arm.
5. Dorsum of hand.
6. Lower abdomen
7. Femoral areas.
8. Knee.
9. Upper abdomen.

These regions of body have increased levels of friction and tension. So, the development of keloid is promoted by this skin tension which also causes development of their specific shape.[7] Keloids located on the anterior part of the chest develop into butterfly shape because of the increased movement of the proximal limb and increased stretching of the area. Whereas keloids over scapula form dumbbell-shaped patterns along the arm's long axis because of the increased stretching force

caused by the arm hanging. Keloids present over the ear lobe develop into rounded shapes because of the motion of the head in circular direction causing stretch forces to develop in this direction during sleep.[7]

❖ NORMAL WOUND HEALING AND HOW ITS DIFFERENT IN KELOID?

Normal wound healing happens after trauma who have no keloid forming tendency and no predisposition; the phases of normal wound healing include:

1. Homeostasis which is the first process happening, which includes vasoconstriction and platelets aggregation to stop bleeding.[2,8]
2. Inflammatory stage where there is recruitment of neutrophils followed by lymphocytes and release of various growth factors like interleukins 1 and 6, transforming growth factors, fibroblast growth factor beta, etc.[9] There is also recruitment of macrophages(M1- proinflammatory ones) which also increase the inflammation. In keloids there is a defect in these macrophages. [9]
3. Proliferation phase where there is proliferation of fibroblasts, increased angiogenesis and granulation tissue formation. If at this stage there is excessive proliferation leads to keloid formation. Keloids have abnormal fibroblasts with there excessive migration and proliferations to site of injury. [8]
4. Remodelling phase, which is the last phase where there is deposition of collagen and ECM. Excessive deposition of these occurs in keloids. [9]

❖ PATHOGENESIS

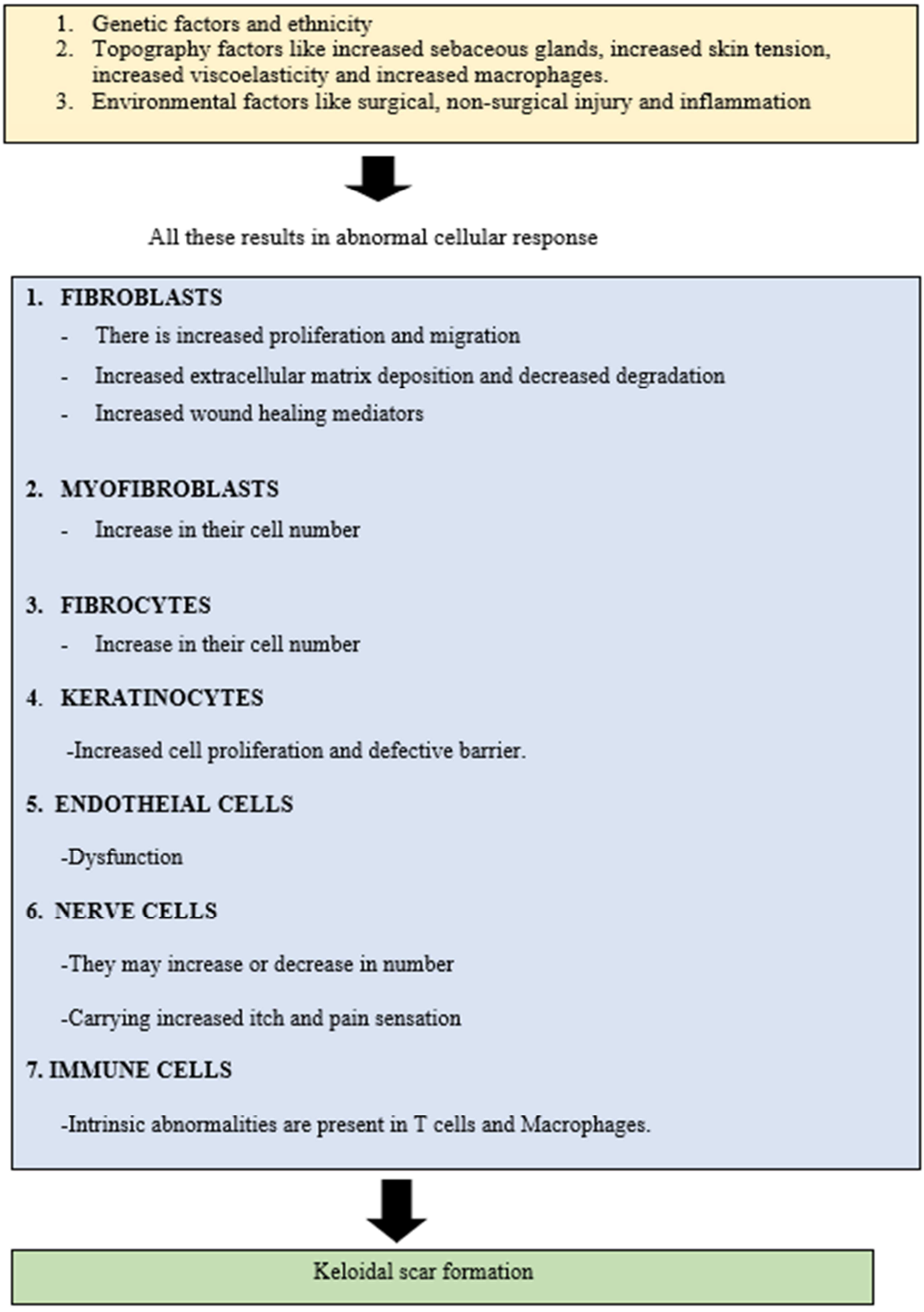


Figure 1. Show the pathogenesis of keloids at cellular level.[8,9]

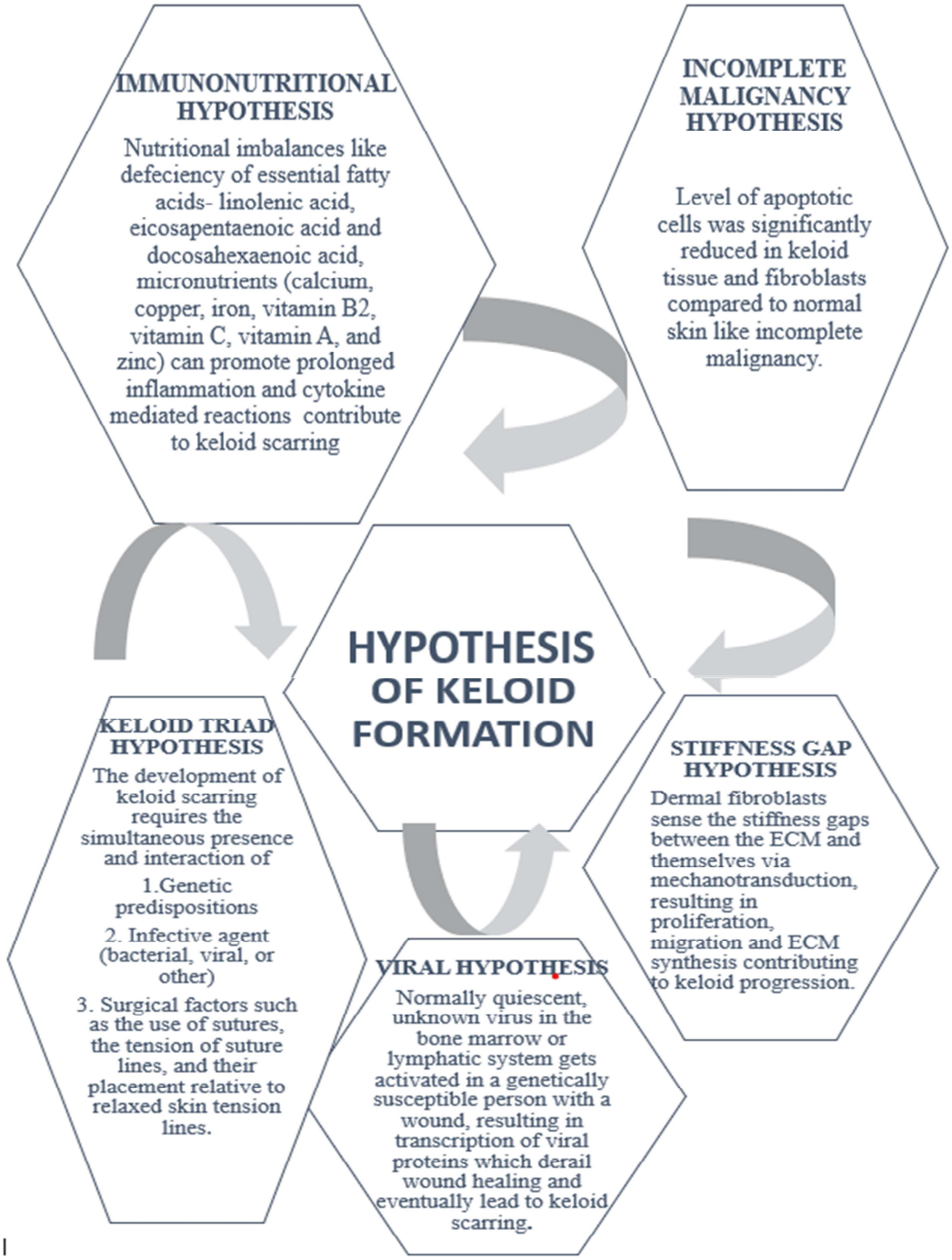


Figure 2. Schematic diagram showing the hypothesis of keloid formation.[10–15]

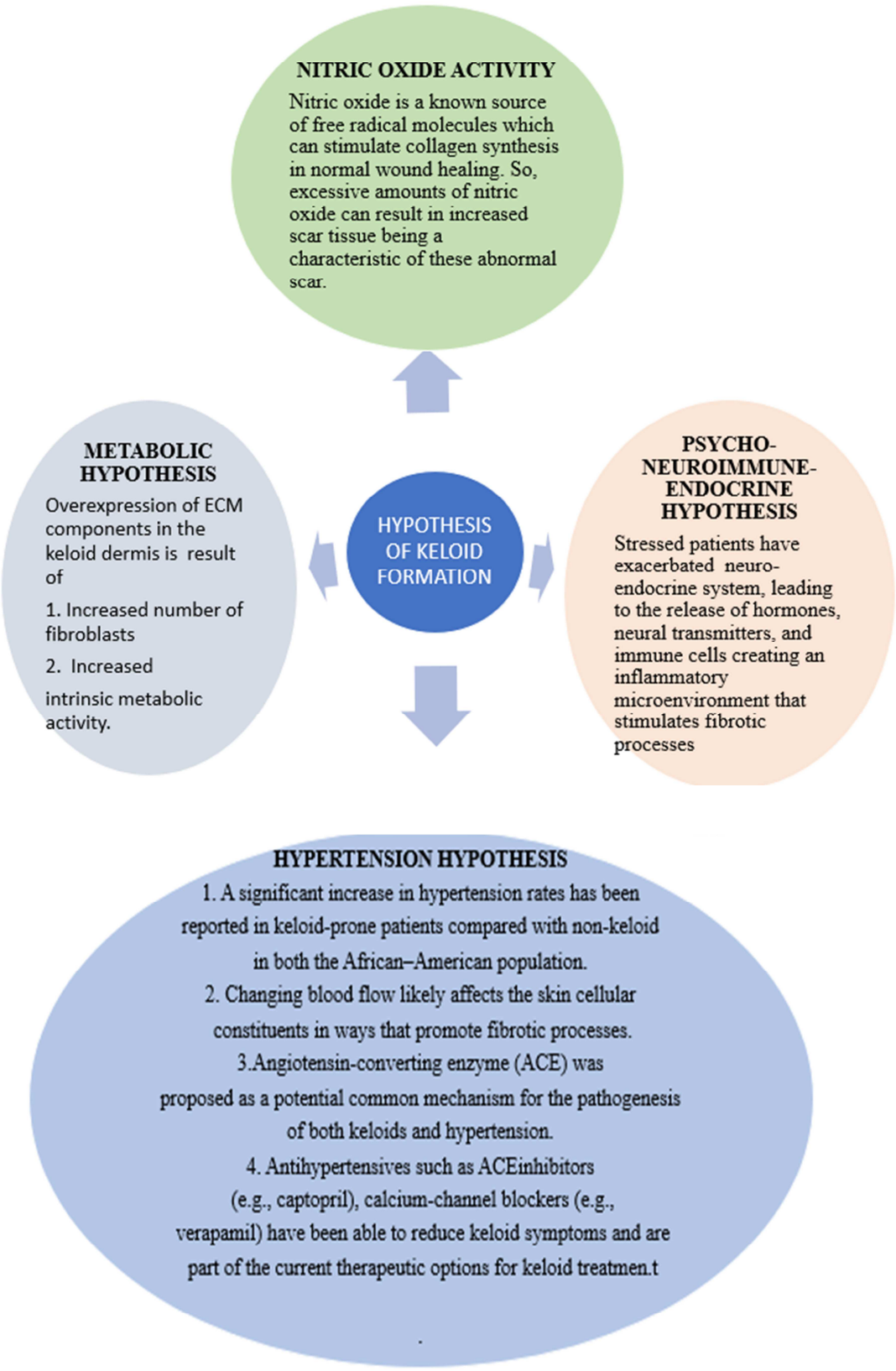


Figure 3. Another hypothesis responsible for keloid formation.[16–20]

❖ CLINICAL FEATURES

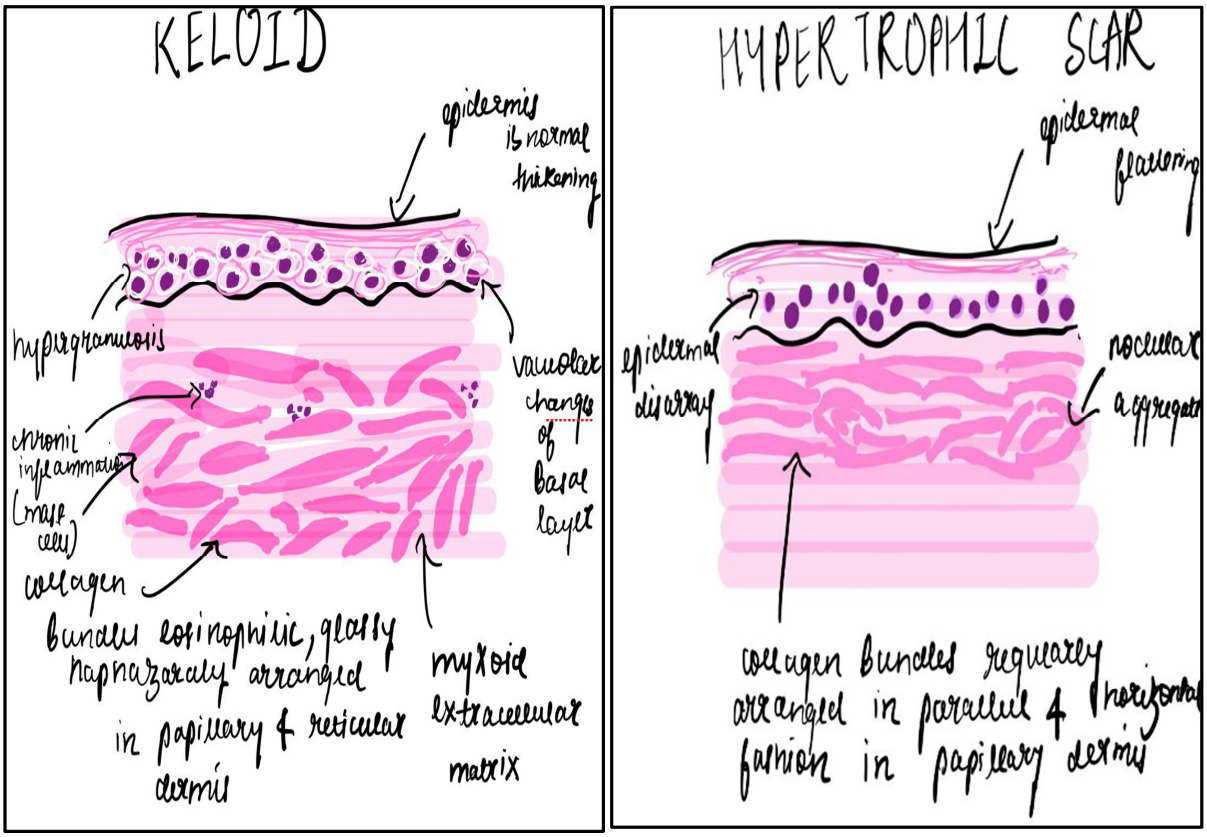
1. A keloid is an overgrowth of tissue containing fibroblast which are densely packed that extends beyond the wound's boundaries unlike hypertrophic scars, which are restricted to the wound's original borders and tend to flatten over time.[21]
2. Keloids are raised and firm.
3. Associated with pruritus and pain, without spontaneous regression.
4. Lee et al. did a study that involved twenty-eight keloid patients found that eighty-six percentage of them reported pruritus, and forty-six percentage experienced pain.[22]
5. In Caucasian individuals, keloids typically appear erythematous and telangiectatic, whereas, in darker-skinned individuals, they are often hyperpigmented. [23]
6. Chest, posterior part of neck, anterior part of chest, earlobes, upper part of back and shoulders are common sites where keloids occur.[23]

❖ DIFFERENTIATION BETWEEN KELOIDS AND HYPERTROPHIC SCAR

	KELOIDS	**HYPERTROPHIC SCAR**
1.Etiology	not always trauma	trauma
2.Stays within confines of injury	no	yes
3.Improvement with time	rarely	yes
4.Symptomatic	Yes, can have pruritis and pain	Yes, can have pruritis not painful
5.Site of occurrence	area of little motion ear lobe, sternal notch, shoulder	area of motion over trauma prone areas
6.Incidence	Rare High recurrence	Frequent Low recurrence
7.Race	blacks	no association
8.Association with surgery	no	yes
9.Response to treatment	variable	good
10.Sodium levels (osmotic pressure)	normal	decreased
11.Magnesium levels (metabolic activity)	increased	decreased
12.Calcium (reflects collagen metabolism)	increased	decreased
13.Mucin	abundant	scanty
14.Fibroblasts	few	numerous
15.Mast cells	increased	increased
16.Foreign body type of reactions	not present	frequently present
17.Stain for collagen (luxol fast blue)	red	blue
18.Myofibroblasts	no	yes
19.Alanine transaminase	increased	normal

20. Alpha-SMA expression	absent	increased
21.Dermoscopy	More vascularity seen	Less vascularity seen
22.Histopathology	1.Smaller fibroblast without myofibroblast, increased proliferation. 2.Thick irregular collagen bundles with haphazard pattern. 3.Type 1 collagen more than type 3 collagen, linkage of collagen more with twenty times more synthesis. 4.Skin appendages – absent glands and hair follicles 5.Do not enter in remodelling phase.	1.Greater fibroblasts and myofibroblast. 2.Arrangement in nodules and parallel with pattern being wavy. 3. Type 3 collagens more than type 1 collagen, less linkage of collagen, with seven times more synthesis. 4. Can have skin appendages – glands and hair follicles 5. Enter in remodelling phase.

Table 1. Shows the difference between keloid and hypertrophic scar.[24–27]



❖ HISTOPATHOLOGY OF KELOIDS

As we go down from top to bottom, we can see the following features in histopathology slide of keloid:[28]

1. Epidermis- Normal thickening of epidermis with rete ridges or flattening.
2. Epidermis can show hyperkeratosis/ hypergranulosis / spongiosis.
3. Basal layer arrangement is regular palliating, less of disarray.
4. Basal layer vacuolar changes can be present.
5. Papillary dermis- scarring.
6. Collagen site- papillary and reticular dermis.
7. Collagen arrangement looks broad and are focally eosinophilic.
8. Collagen cellularity- numerous and acellular.
9. Horizontal fibrous bands in upper reticular dermis- prominent.
10. Myxoid extracellular matrix- present.
11. Orientation of blood vessels- aggregating below the epidermis.
12. Chronic inflammatory infiltrate- present with mast cells.

❖ HISTOPATHOLOGICAL DIFFERENTIAL DIAGNOSIS OF KELOIDS

1. Morphea- Has increased collagen in dermis, sclerosis and perivascular lymphocytic infiltrate.[25]
2. Hypertrophic scar

❖ MIMICKERS OF KELOIDS

1. Squamous cell carcinoma.
2. Dermatofibrosarcoma protuberans.
3. Pilomatricoma.
4. Nodular Scleroderma.
5. Lobomycosis.
6. Cutaneous psuedolyphoma.

❖ TREATMENT OF KELOIDS

1. INTRALESIONAL THERAPY	- **INTRALESIONAL TAC** - **INTRALESIONAL VERAPAMIL HYDROCHLORIDE.** - **INTRALESIONAL 5-FLUROURACIL** - **INTRALESIONAL BLEOMYCIN** - **INTRALESIONAL BOTULINUM TOXIN A** - **TRIPLE COMBINATION** - **INTRALESIONAL METHOTREXATE** - **INTRALESIONAL INTERFERON-ALPHA 2b** - **INTRALESIONAL TGF-BETA 3** - **INTRALESIONAL MITOMYCIN C**
2. TOPICAL THERAPY	- **SILICONE SHEETS** - **SILICONE GELS**

	- **ALLANTOIN WITH HEPARIN WITH EXTRACTUM CAPEA** - **SILICONE GELS WITH CYCLOMETHICONE NF-5, CERAMIDE, POLYDIMETHYLSILOXNANE TECHNOLOGY AND PRO VITAMIN C.** - **ONION EXTRACT** - **CAPTOPRIL CREAM** - **IMIQUIMOD CREAM** - **TACROLIMUS OINTMENT**
3. CRYOTHERPAY	- **BY LIQUID NITROGEN CRYOSPRAY** - **INTRALESIONAL CRYOTHERAPY**
4. LASER	- **IPL LASER** - **FRACTIONAL CO2 LASER** - **ABLATIVE CO2 LASER** - **MNRF FOLLOWED BY STEROID OCCLUSION**
5. SURGERY	- **EXCISION FOR ONLY EAR LOBE KELOIDS**
6. NEWER MODALITY	- **INTRALESIONAL RADIO FREQUENCY ABLATION** - **PRESSURE GARMENT**

Table 2. Shows different treatment modalities for keloids.[29]

❖ INTRALESIONAL TAC-

1. MECHANISM OF ACTION

- Corticosteroids inhibits the activation and migration of monocytes and also leukocytes as well as their ability to perform phagocytosis, thus suppressing the inflammatory process.[30]
- Acts as potent vasoconstrictors, which limits the oxygen delivery and nutrients to base of wound. [31]
- Exhibit anti-mitotic effects thus inhibiting the activity of keratinocytes and fibroblasts ultimately leading to decrease in re-epithelialisation and collagen synthesis.
- Reduce alpha-2-macroglobulin and alpha-1-antitrypsin which are inhibitors of plasma protease and—natural inhibitors of collagenase—allowing collagenase to degrade collagen more effectively, which are often elevated in keloidal tissue.[32]
- Inhibit fibroblast proliferation and their capacity to produce collagen, contributing to their degeneration.
- Decrease levels of tissue growth factor-beta, hydroxyproline and IGF-1 in scar tissue. [33]
- Expression of vascular endothelial growth factor, and proliferation of fibroblasts is suppressed.

2. RESPONSE RATES-

- Response to corticosteroid injection - 50–100% regression[34]
- Recurrence rate of 33% after 1 years and 50% at 5 years.[34]

3. DOSAGE-

- There dosage of steroids, the duration of treatment given and the frequency differed among various practitioners:

Rahban and Garner et al[35]	Dose - 10 mg/mL, 4 to 8 weeks apart.
Darzi et al[36]	Dose - 20–40 mg, area 1-2 cm^2 Dose- 60-80 mg, area 2–6 cm^2 Dose-80–120 mg, 6–12 cm^2
Robles et al[37]	trunk or extremities- 10 to 40 mg/mL

Table 3: Shows the dosage of intralesional Triamcinolone Acetonide therapy for keloids according to site and area.

4. SIDE EFFECTS

LOCAL EFFECTS-	- Skin atrophy. -Subcutaneous fat atrophy. -Telangiectasia. -Hyperpigmentation. -Hypopigmentation. -Necrosis of skin. -Ulceration

SYSTEMIC EFFECTS-	-Adrenal insufficiency. -Cushing's syndrome. -Gain of weight. -Depression. -Hyperglycaemia. -Moon facies. -Amenorrhea. -Striae rubrae.

Table 4: Shows the side effects of intralesional TAC therapy for treatment of keloids.[38]

For injection,

1. Needle of sixteen millimetre and twenty-five gauge was used because it requires the lowest amount of injection force.[39]
2. It is most widely used for injecting different modalities intralesional into the keloids.

5. CONTRAINDICATIONS-

- Uncontrolled diabetes mellitus.
- Bleeding disorder
- Immunosuppression

❖ INTRALESIONAL VERAPAMIL HYDROCHLORIDE

1. MECHANISM OF ACTION

1. Verapamil is a calcium channel blocker which enhances the procollagenase synthesis in keloids, hypertrophic scars, and normal human fibroblasts and also causes the actin filaments to depolymerize.[40]
2. It brings about a change in the cell morphology to a spherical shape from its normally existing shape which is bipolar, and a subsequent reduction in fibrous tissue production.
3. Decorin production is increased which is a molecule having various effects on fibroblasts such as reduced migration and proliferation and apoptosis is increased. [41]
4. Production of VEGF and IL-6– suppressed. Levels of these are generally found to be elevated in keloid fibroblasts. [41]
5. Secretion of components such as glycosaminoglycans, collagen and fibronectin, which are a part of extra cellular matrix is inhibited leading to decreased fibroblast proliferation, enhanced apoptosis, and reduced scar tissue formation.[41]
6. It also slows action potential conduction, resulting in reduced pain and itching. [42,43]

2. DOSAGE-

- It is given intralesional with the help of insulin syringe at a dosage of 2.5 mg/ml.
- Can be also combined with TAC for the intralesional therapy for keloids treatment, injected at a ratio of 1:1 of TAC concentration of 40 mg/mL and verapamil concentration being 2.5 mg/mL, injecting only 0.1 millilitre of it.[44]

3. SIDE EFFECTS-

LOCAL	• Pain while injecting • Telangiectasia, atrophy and hypopigmentation was not seen with intralesional verapamil hydrochloride, which was seen in intralesional triamcinolone.
SYSTEMIC	• Nausea • Headache • Dizziness • Hypotension

Table 5: Shows the side effects of intralesional verapamil hydrochloride therapy for keloids.[38]

❖ **INTRALESIONAL 5-FLUROURACIL**

1. MECHANISM OF ACTION

1. 5-fluorouracil, a pyrimidine analogue, disrupts deoxyribonucleic acid synthesis by irreversible inhibition of thymidine synthase enzyme which is responsible for conversion of uridine into thymidine base. This inhibition prevents the formation of essential components required for biosynthesis, effectively halting the proliferation of rapidly dividing cells like fibroblasts and helping in decreasing keloid size. [45]
2. It also suppresses the expression of type I collagen gene and the activity of transforming growth factor beta-1.[45]
3. The reduction of proliferation of fibroblast in keloid is dependent on the dosage of 5-FU.
4. It also inhibits type I collagen gene expression and the effects of tumor growth factor-beta.

2.DOSAGE-

- 5-fluorouracil comes at a dosage of 250 mg/5ml, and 50 ml is given intralesional.
- Can be combined with triamcinolone acetonide. The ratios of 5-FU to TAC most commonly used are 1:9 or 1:3.[45]
- Protocols vary significantly in the intervals between treatment sessions, ranging from weekly to every four weeks.

3. SIDE EFFECTS-

- Pain
- Hyperpigmentation
- Ulceration

❖ **INTRALESIONAL BLEOMYCIN**

1. MECHANISM OF ACTION

- Bleomycin-induced apoptosis and cause sclerosis of endothelial cells.
- It inhibits- lysyl oxidase enzyme, thus decreasing synthesis of collagen.[46]
- Downregulates Tissue growth factor-beta.

2. DOSAGE-

- A bleomycin injectable solution can be prepared by diluting fifteen units of bleomycin in ten millilitres of normal saline, which has to be sterile.[47]
- This solution is then administered at a depth at the centre of the keloid injecting-0.2–0.4 millilitre per cm^2. The maximum volume that can be injected is 3.5 millilitre.[48]

3. SIDE EFFECTS-

- Persistent pain after injection.
- Ulceration
- Hyperpigmentation
- Secondary infection.

❖ INTRALESIONAL METHOTREXATE

1. MECHANISM OF ACTION

It inhibits dihydrofolate reductase which causes reduction of dihydrofolate to its active form leading to its anti-proliferative and anti-inflammatory action and thus inhibits the activity and proliferation of these fibroblast cells causing reduction in the volume of keloids. [49]

2. DOSAGE-

15 mg intralesional can be injected. Require more studies on the side effects associated and efficacy.

❖ INTRALESIONAL BOTULINUM TOXIN A

1. MECHANISM OF ACTION	It blocks the action of proteins SNARE – which is required for fusion of plasma membrane with the synaptic vesicles containing acetylcholine in turn causing decrease in the cholinergic transmission in neuromuscular junction and smooth muscle. - It also temporarily denervate smooth muscle fibres, reducing tension within the scar tissue—an important factor influencing the extent of scar formation.

	- It relieves scar tension and promotes a gradual shift in the activity of local fibroblasts, 1. to proliferate more slowly 2. secrete fewer biologically active mediators 3. produce less extracellular matrix and collagen. This process ultimately results in the improvement of hypertrophic scars.
2.DOSE	Botulinum toxin A 100 units containing vial is diluted ⬇ It is to be diluted with two millilitres of 0.9%normal saline which needs to free of preservative free ⬇ It is to be constituted at a concentration being- **4 U/0.1 millilitre.** ⬇ It is to administered monthly once for three such months ⬇ By using Nine-gauge needle it is injected into the keloid with endpoint being little blanching ⬇ Per session it shouldn't exceed more than 100 units and the dose is injected 2.5 units per centimetre cube.
3.BENEFITS	-Has lower incidence and severity of pain compared with patients who received intralesional injections with corticosteroid. -There is improvement in the appearance of keloid with reduction of redness, itching associated with keloid and also induration.

Table 6: Shows the mechanism of action, dose and benefits of intralesional botulinum toxin A therapy for keloids.[50–54]

❖ TRIPLE COMBINATION OF KELOIDS

1. MECHANISM OF ACTION

1.5-fluorouracil (an antimetabolite that suppresses fibroblast proliferation)

2. Triamcinolone acetonide (an anti-inflammatory agent)

3.Hyaluronidase (an agent that has been shown to dissolve fibrous bands).

Figure 4: Shows the mechanism of action of the triple combination constituents. [55]

2. PROCEDURE

A 1mL solution was prepared by aspirating:

- 0.6mL from a 5mL ampoule of 5-fluorouracil (250mg/5mL).
- 0.4mL from a 1mL vial of triamcinolone acetonide (40mg/mL).

↓

These were then injected into a vial containing a vacuum-dried bovine-origin hyaluronidase (1500 units).

↓

The vial, with the three agents incorporated, was shaken vigorously for several minutes to ensure adequate mixing of the components.

↓

The mixture was then aspirated into a 2mL syringe using an 18-gauge needle. The triple combination mixture was injected into the body of the scar using a 26-gauge needle.

↓

Patients with larger or multiple scars required more than one 1mL injection at each visit to cover the entire affected scar area.

Figure 5: Shows the procedure of triple combination for keloids treatment. [55]

❖ SILICONE CONTAINING GELS

MECHANISM OF ACTION

1. The cytokine production is influenced by the water content of stratum corneum which is increased by silicone which further leads to decrease in IL-8 and fibronectin levels.[56]
2. It also reduces fibronectin concentration.
3. Does not completely eliminate keloids but plays a significant role in modulating their formation, helping to reduce thickness and firmness. [56,57]
4. Improve texture, followed by pigmentation, and then reduce height of keloid.[57]

FREQUENCY OF APPLICATION

1. Silicone gel sheeting is to be applied after the complete reepithelization has happened for at least 12 hours daily for a period of 2- 3 months. [58–60]
2. This therapy has minimal adverse effects and can be used as a preventive measure for individuals prone to hypertrophic scars or keloids, as well as combination with other treatments. Gel form of silicone is easy and convenient to use.[60,61]
3. Post operation you can use the gel sheeting of silicone once the reepithelialisation been completed and is ineffective if used once it has not happened. [60,61]
4. Combination of - 0.5% hydrocortisone, vitamin E and silicone is also effective.[61]

- **GEL CONTAINING HEPARIN SODIUM-ALLANTOIN-CPEA EXTRACTUM COMBINATION-**

1. This combination has entered the standard treatment guidelines for treating keloids and hypertrophic scars.[62]

2. It has anti-inflammatory and anti-fibrotic properties.

- **CRYOTHERAPY**

MECHANISM OF ACTION.

1. It also causes transition of fibroblast of keloids to how the normal fibroblast of skin behaves and also increases the type three to type one collagen ration in the keloid.[63]
2. Preservation of the decellularized matrix, which may serve as a scaffold to help prevent recurrence.
3. It causes cellular damage through cryonecrosis, a process involving intra- and extracellular ice formation, osmolarity changes, thermal shock, and lipoprotein complex denaturation.[64]
4. Significant mechanism in keloid treatment is ischemic necrosis, caused by microthrombi formation and vascular stasis.[64,65]
5. Modulates the immune response, triggering apoptosis in tumor cells.[65]

1. PROCEDURE

CRYOSPRAY	INTRALESIONAL CRYOTHERAPY
1. Liquid −79 °C spray-type CryoPen. 2. Two freeze thaw cycle of 15 seconds freeze time using spot freeze technique. 3. Once a month session. 4. Advantage of combining 5-FU with cryotherapy is its side effect of hyperpigmentation, which counteracts the hypopigmentation caused by cryotherapy, resulting in improved overall cosmetic outcomes.	1. With the help of circular motion, the probe is inserted completely till it completely` penetrates the keloidal tissues opposite end. 2. Once in place, liquid nitrogen source is connected to probe's proximal end, allowing gas to flow through the needle. 3. The freezing process is carried out until the keloidal tissue appears adequately frozen after visual assessment of it, usually taking 10 minutes to 1 hour, depending on the size of the scar. 4. After allowing a thawing period of about 60 seconds, the probe is carefully withdrawn, and the treated area is covered with an antibiotic cream and sterile gauze piece.

Table 7: Shows the procedure of cryospray and intralesional cryotherapy.[64,65]

2. SIDE EFFECTS

It can lead to pain, ulceration, blister formation and hypopigmentation of the treated area.

❖ **RADIOTHERAPY AND SURGICAL EXCISION**

1. Surgical excision can be done for keloids, when first-line therapies have proven ineffective. However, when used as a stand-alone treatment there is a recurrence of 100%.[60]

2. To mitigate this risk, combination therapies have been implemented such as Surgical excision radiotherapy can be used which works by

- Inhibiting proliferation of keloids by TGF-beta downregulation.
- Reducing the histamine release from mast cells. [60]

3. Common side effects include telangiectasia, scarring and depigmentation.

4. Surgical excision is mostly used for keloids present over earlobe, but is found to be ineffective for keloids present over different areas.

❖ PHOTODYNAMIC THERAPY

Although evidence remains limited, research on the use of photodynamic therapy (PDT) is increasing. PDT is performed after topically applying like 5-aminolevulinic acid, a photosensitiser in turn followed by irradiation by LED. While the exact mechanisms behind its effects on keloids are still being explored, PDT is gaining recognition as a adjunctive therapy for keloid management.[60]

❖ LASER

ABLATIVE LASERS	
1. Erbium (Er: YAG) laser	2940 nm Erbium Yag laser (Fractional ablative laser) can help in enhancing the delivery of-betamethasone ointment for treatment of keloid.
2. Carbon-dioxide laser ablation	• It targets the chromophore that is water and cause reduction in keloidal tissue. • For firm keloids you should use super pulse mode and for hard keloids continuous mode with a power of fifteen watt It should be excised from the keloidal base.

	• Up to the level of upper part of reticular dermis it should be ablated which can be indicated by the change of colour to light brown and yellow. • After ablation of keloid intralesional triamcinolone acetonide 40mg/ml can be injected in the periphery at intervals of 3 weeks for a period of 6 months. • It can be used as independent treatment for keloid and also can be used as combination therapy. It can help in the delivery of drug and enhance their penetration.
NON-ABLATIVE LASER	
1. Pulsed dye lasers (PDL)	• Wavelenght being 585 nanometres. • Targets haemoglobin and helps in reduction of vascularity of keloids, causes suppression of fibroblast damages the blood vessels present in the keloid. Wavelenght being 585 nanometres. • Reduces the symptoms of pruritis associated with keloids and also cosmetic appearance of keloids is improved. • It can be combined with other intralesional therapy which is more effective than using it alone. • Has a limited use in keloids which are thick as the depth of penetration is just 1.2 millimetre. • Resolve scar-associated symptoms such as pruritus.
2. ND:YAG laser	• It causes reduction of the keloid's vascularity, growth factors and cytokines which then cause reduction of deposition of collagen in the tissue. • Treatment setting- 1. Spot. diameter -5 mm. 2. Energy. density -75 J/cm2 3. Exposure time - 25 ms 4. Rate- 2Hz

3. Diode lasers and LED phototherapy	• Targets melanin. • Uses 805-nm (near infrared light) a LED phototherapy can be used for keloids by preventing its development. Can be used for keloid patients after excision or CO2 laser ablation of keloids.
4. IPL laser	• IPL laser parameters - Vascular filter. - 530-650 and 900-1200 nm - Fluence. -22-24 J/cm2 - Pulse duration - 4-5 ms with double-pulse - Pulse delay - 30-40 ms. • Endpoint when colour of keloid becomes dark red or light grey. • Done at 4-week intervals • Side effects – causing. burns, reduction in the pain, blister formation. which can lead to crusting. and can also cause pigmentation.

Table 8: Shows the use of various laser for treatment of keloids.[61,66–69]

❖ **INTRALESIONAL RADIO FREQUENCY ABLATION-**

a. The intra-lesional RFA technique is a newer modality of treatment for reduction in the size of keloids with procedure being-

(a) An 18-gauge intravenous cannula featuring a small opening in its plastic sheath near the proximal end, close to the hub whereas the distal 0.5 cm of the metallic needle is exposed by removing the plastic covering.[70]

(b) RFA probe is inserted to be in contact with the metallic needle through the designated opening in the plastic cannula.[70]

b. (c) The effects of RFA coagulation are visible as pallor and wrinkling of the skin over the keloid.

This modality cause reduction in the volume of keloids up to half of its volume. It can also cause reduction in the erythema, pliability of keloids. There can also be reduction in the symptoms of patients associated with keloids like pruritis and pain. The side effects such as pain post procedure is variable. Mostly the side effects found in studies are ulceration and blister formation. The recurrence rate of keloid formation is reduced and cosmetic results are also good.[71]

❖ **INTRALESIONAL INTERFERON-ALPHA 2b**

IFN-alpha 2b is a cytokine whose levels are decreased in keloid tissue, which inhibits the proliferation of fibroblasts and increases the breakdown of collagen. It also decreased the angiogenesis in keloids. It is used at a dose of 0.5 million units per centimetre square area of keloid, available as 1 million units per 0.1 ml, which can be given twice weekly. [72] It causes reduction in the size of keloids. Can be used as combination therapy with TAC. Side effects are pain at the site of injection, flue-like symptoms which includes fever and chills, can also lead to hyperpigmentation or hypopigmentation.[73]

❖ **OTHER TREATMENTS-**

1. **Pressure garment therapy**- It can be used for 6 months to 2 years. Can be kept for at least twenty-three hours a day with 24-30 mmHg pressure is recommended. But it can decrease the pruritis and pain symptom of keloids, but not that cost effective.[74]
2. **Onion extrac**t- Quercetin is a onion extract, is a flavonoid which causes inhibition of proliferation of fibroblast and decreases the collagen production. It also reduces the pruritis symptoms by its anti- histamine property.[74]
3. **Intralesional Mitomycin C-** It also inhibits the fibroblast proliferation and also DNA and RNA synthesis. Requires more research in this field.[74]

4. **Angiotensin converting enzyme inhibitor**- Captopril 5% cream and oral Enalapril have effect on collagen synthesis so can be used for keloid treatment.[74]
5. **Transforming growth factor beta- 3-** Avotermin is available and can be injected intradermally over keloid tissue. It has no side effects. Can cause erythema and edema.[74]
6. **Tacrolimus**- It is a calcineurin inhibitor and causes immunosuppression. It reduces the migration and proliferation of fibroblasts and decreases the collagen production and reduces the scar formation. Requires more research.[74]
7. **Imiquimod-** It is a Toll-like receptor agonist, imiquimod enhances the production tumor necrosis factor-α and pro inflammatory cytokines like interleukins 1, 6, 8 and also the expression of genes responsible for apoptosis within keloid tissue is enhanced. Available as 5% cream formulation and mainly used to prevent the recurrence of keloid post surgery. Side effects being hyperpigmentation. skin irritation with crusting and erosion.[74]

❖ SCORING SYSTEM FOR KELOIDS

1. Vancouver. scar scale (VSS)-	Consisting of pliability, vascularity, height and pigmentation as parameter. Most widely used scale in studies. Minimum score is 0 and maximum score is 13.
2. Patient and observer scar assessment scale (POSAS)-	Consisting of pain, itching, colour, thickness, flexibility, vascularity, pigmentation, surface area and surface relief as parameters. Score has a range from 0-60.
3. Keloid Area and Severity Index (KASI)	It consists of activity index which consist of Erythema and suppuration and damage index which consist of elevation, body surface area involved and location.
4. Detroit Keloid Scale.	It consists of location, height and surface area. Maximum score is 6.
5. Japan Scar Workshop scale(JSW).	It helps in assessing the risk factors of keloids and can help in differentiating keloids and hypertrophic scar based on genetic, local and systemic factors.

Table 9: Shows the various scoring system used for keloids [75–77]

MATERIALS AND METHODS

- **Study source:** This study was conducted. in department of dermatology, venereology and leprosy. A tertiary care hospital, Belgaum as a part of MD program academic circular.
- **Study duration:** This study was conducted in the duration 1st April 2023 to 31st march 2024 (one year).
- **Ethical clearance:** Clearance was taken from Institutional ethical committee. Reference number: **NDC/JNMCIEC/106**
- **CTRI registration:** CTRI registration was done for the study. CTRI number- **CTRI/2024/01/161273.**
- **Study Design:** This study is open label, non-randomized, interventional study comparing triamcinolone and verapamil in treatment of keloids.
- **Sample**. **Size:** The formula used for sample size calculation is,

$$n = \frac{2\,(Z_{\alpha/2}+Z_{\beta})^2}{d^2}$$

$$where,\ d = \frac{(|\mu 1-\mu 2|)}{\sigma}$$

Where, μ1. is mean of the first group, μ2 is mean of the second group, $\sigma 2$. is the common error variance, $Z\alpha_{/2}$ value is 1.96 for 95% confidence level and Z_{β} value is 1.0364 for 85% power. Assuming high between group effect size of difference in VSS scores from baseline to final follow-up (d = 0.8), at 5% level of significance and 85% power, the total sample size required is 30 patients having 2 keloids each. Considering 10% follow up loss, the total sample size will be 33 patients. As sample size increases, the accuracy of result also increases. Value of d is assumed.

Sample size = 33

- **Sampling**. **technique:** convenient. sampling is used.
- **Inclusion**. **Criteria:**
    1. Keloid patients aged between 18 and 70 years old.
    2. Patients having more than or equal to two keloids.
- **Exclusion**. **Criteria:**
    1. Patients with evidence. of any infection (in or near the scar area)
    2. Patient with a history of cardiovascular. problems and pregnant women.
    3. Patient received any intralesional over keloids in past 1 months.
    4. Patient who didn't give informed consent for this treatment.
- **Discussion:**

1. The patients diagnosed with having more than or equal to two keloids attending KLES Dr. Prabhakar hospital and medical research Centre were recruited for the study.
2. Informed consent would be taken from the patient who has fulfilled our inclusion criteria
3. All the patients in the study will undergo detailed history taking, general physical examination, systemic and dermatological examination. Data will be collected by single examiner and recorded in case record proforma.
4. Patients will be All explained about the treatment offered in terms of procedure done, expected results, duration of treatment, follow up and side effect profile.
5. Digital photograph of the 2 Keloids of the patient will be taken using identical camera setting and room lightening before the start of treatment and at the end of 9 weeks.

6. Two keloids are selected in which first keloid will receive intralesional triamcinolone and second keloid will receive intralesional verapamil. Vancouver scar scale. (VSS) will be used for analysis. The mentioned scale scores the scars on 4 parameters: height, vascularity, pliability, and pigmentation. Height of keloids is accurately measured with a ruler in millimeters. Scar vascularity and pigmentation will be assessed by visual inspection. Scar pliability is subjectively assessed by palpation.
7. First keloid is given intralesional triamcinolone acetonide and second keloid is given intralesional verapamil. The injections are given with the help of insulin syringe.
8. Vial of TAC having 40mg/ ml is taken and is diluted with lignocaine. First keloid received intralesional triamcinolone acetonide, maximum of 1ml is given, every 3 weeks for 9 weeks (3 sessions)
9. Second keloid receives intralesional verapamil hydrochloride (2.5 mg/ ml)1ml every 3 weeks for 9 weeks (3 sessions)
10. Scoring is done one before the first injection and other at 9 weeks by Vancouver scar scale (VSS). Visual analogue scale is also used for the analysis according to patient satisfaction calculate at baseline and at the end of 9 weeks. VAS pruritis score and numeric pain rating score is used to calculate the pruritis and pain associated with keloids at 0 weeks and at the end of 9 weeks.
11. Safety between two treatment modalities is compared and the numeric pain rating scale while injecting TAC and verapamil is also calculated at the third session and change in various parameters like reduction in height, changes in vascularity, pigmentation and pliability of keloids and volume reduction of keloids between these two treatment modalities is compared at the end of 9 weeks.

Statistical analysis:

The data analysis will be conducted using statistical software, specifically R version 4.2.1.and Microsoft Excel. Categorical variables will be presented using frequency tables, while continuous variables will be expressed as Mean ± SD or Median (Min, Max). The Chi-Square test. will be applied to assess associations between categorical variables.

The normality of the data will be evaluated using the Shapiro-Wilk.test. If the data follow a normal distribution, parametric tests will be employed; otherwise, non-parametric tests will be utilized. The Mann-Whitney U test will be used to compare the means or distributions between two independent groups. To analyze differences between two time points (pre-treatment and post-treatment follow-up), either a paired t-test or the Wilcoxon signed-rank test will be used, depending on normality.

Relevant tables and figures will be generated for clarity. Graphical representations, including pie charts and bar diagrams, will be used for visualization. A p-value of ≤ 0.05 will be considered statistically significant. Additionally, the paired t-test will be applied to compare changes in height, vascularity, pigmentation, pliability, and volume between the two treatment approaches.

RESULTS

In our study 33 patient with more than equal to two keloids were included. Patients with age group falling between 18-70. Years of age were included in the study. The mean age of the patients recruited was 37.24 years.

Age group(years)	Number	Percentage
18-27	17	51.51%
28-37	3	9.09%
38- 47	1	3.03%
48-70	12	36.36%

Table 10: Distribution of study participants by age (years).

Among the study participants majority of the participants fall into the category of 18-27 years with percentage being 51.51%. The next category of age group was participants being in the age group of 48-70.years representing 36.36% of the sample population. The age group between 38-47 years represented 3.03% of the sample size, which was the least. The age group of 28-37. years represented 9.09% of the sample size population. The mean age was 37.24 years, standard deviation was 18.17 years. The minimum. age of the study participant was 18 years and maximum age was 67 years. The median. of our study was 27 years.

	Mean	Standard Deviation	Median	Minimum	Maximum
AGE	37.24	18.17	27	18	67

Table 11: Shows the mean age, median, minimum and maximum age of study participants.

In our study, out of a total of 33 patients, 24 were males, making up 72.73% of the sample population, while 9 were females, accounting for 27.27%. The results clearly show that males outnumbered females in this sample.

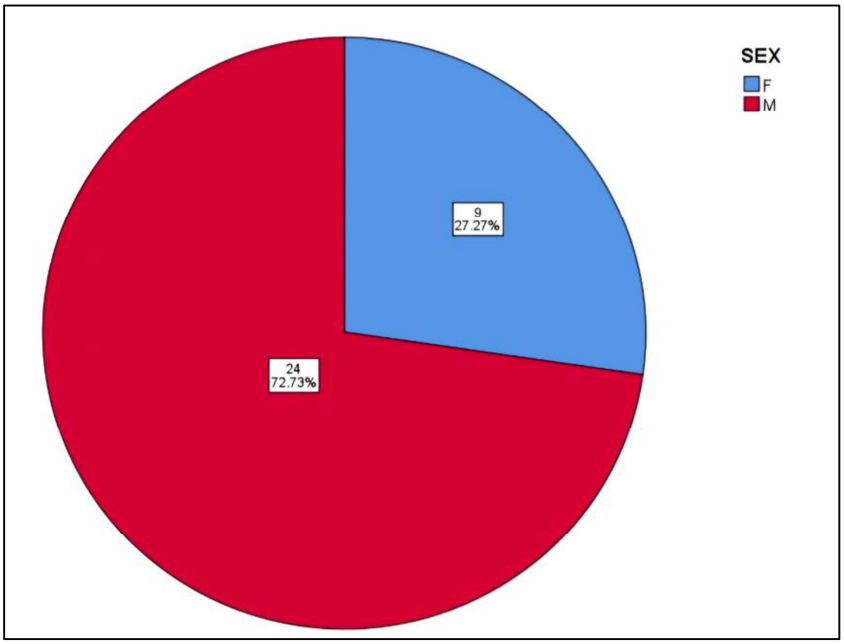


Figure 6: Shows pie diagram representing the gender distribution of the patients recruited in the study.

SEX	Frequency	Percent
F	9	27.3
M	24	72.7
Total	33	100

Table 12: Shows the frequency and percentage distribution among the males and females in our study.

In our study, the aetiology of keloids among participants was categorized into several factors: surgery, acne, trauma, shaving, radiotherapy, and unknown causes. The most common aetiologies were surgery and acne, each accounting for 27.2% of the participants. This was closely followed by cases with unknown aetiology, which made up 18.18%. Trauma and shaving were identified as the second least common causes, each contributing to 12.12% of the cases. The least frequent cause was radiotherapy, which was responsible for just 3.03% of the participants.

cause of keloids	acne	18	27.27%
	radiotherapy	2	3.03%
	shaving	8	12.12%
	surgery	18	27.27%
	trauma	8	12.12%
	unknown	12	18.18%

Table 13: Shows the frequency and percentage distribution among the males and females in our study.

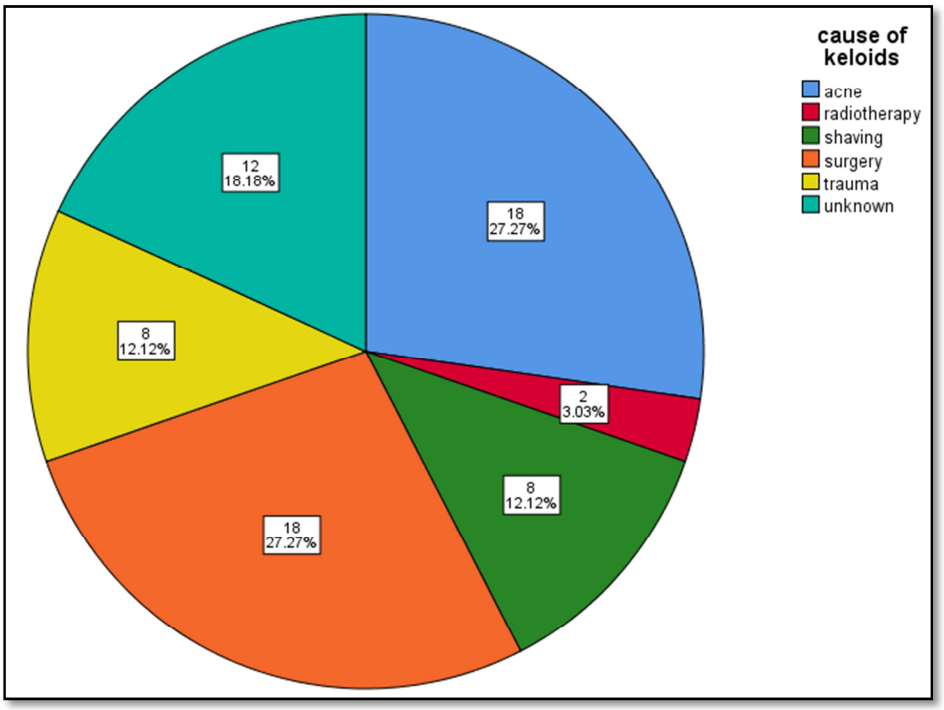


Figure 7: Shows pie diagram representing the aetiology for keloids among the study participants recruited in the study.

The majority of keloids in this study were located on the **anterior chest**, affecting **57.58%** of cases. The **upper arm** was the second most common site, accounting for **21.21%.** Other locations included the **breast** and **dorsum of the hand**, each making up **6.06%** of cases. Less frequently, keloids were found on the **arm, back, and scapular region**, with each of these sites representing **3.03%** of occurrences.

This distribution highlights the tendency of keloids to develop on areas prone to tension and movement, which may contribute to their persistence and recurrence.

		Count	Percentage
location of keloid	anterior chest	38	57.58%
	arm	2	3.03%
	back	2	3.03%
	breast	4	6.06%
	dorsum of hand	4	6.06%
	scapular	2	3.03%
	upper arm	14	21.21%

Table 14: Shows the location of keloids among the study participants.

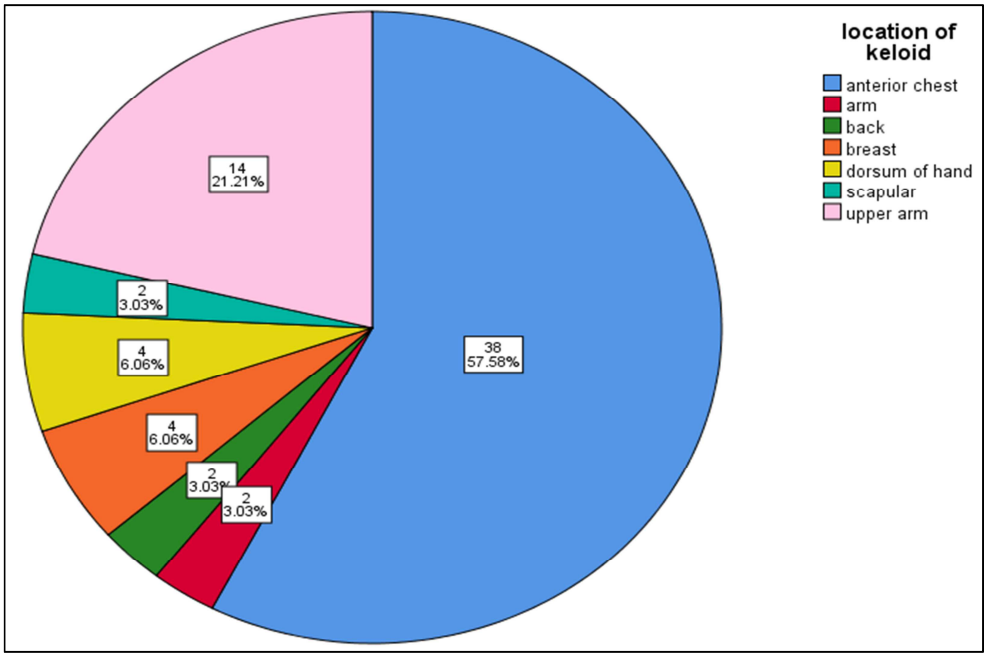


Figure 8: Pie diagram showing location of keloids among the study participants.

For assessment of efficacy between Triamcinolone and Verapamil injection for keloids Vancouver scar scale was used which consisted of parameters being – vascularity, .pigmentation, pliability and height.

VANCOUVER SCAR SCALE	SCAR CHARACTERISTIC	SCORE
VASCULARITY	NORMAL	0
	PINK	1
	RED	2
	PURPLE	3
PIGMENTATION	NORMAL	0
	HYPOPIGMENTATION	1
	HYPERPIGMENTATION	2
PLIABILITY	NORMAL	0
	SUPPLE	1
	YIELDING	2
	FIRM	3
	ROPES	4
	CONTRACTURES	5
HEIGHT(mm)	FLAT	0
	<2	1
	2-5	2
	>5	3

Table 15: Shows the Vancouver. scar scale for measurement of efficacy.

The mean score of vascularity was 2.46 in the Triamcinolone group at 0 weeks that is at baseline and the mean score of vascularity in the Verapamil group was 2.36. At the end of 9 weeks, vascularity score decreased to 1.21 in the Triamcinolone group and 1.3 in the Verapamil group, showing both the groups effective in reducing the vascularity of keloids. Both the groups caused significant reduction in the vascularity scores of keloids. There was no significant. difference between both the groups in terms of vascularity parameters. It was also found in the study that verapamil group was more effective in reducing vascularity of keloid and works better in keloids associated with more vascularity.

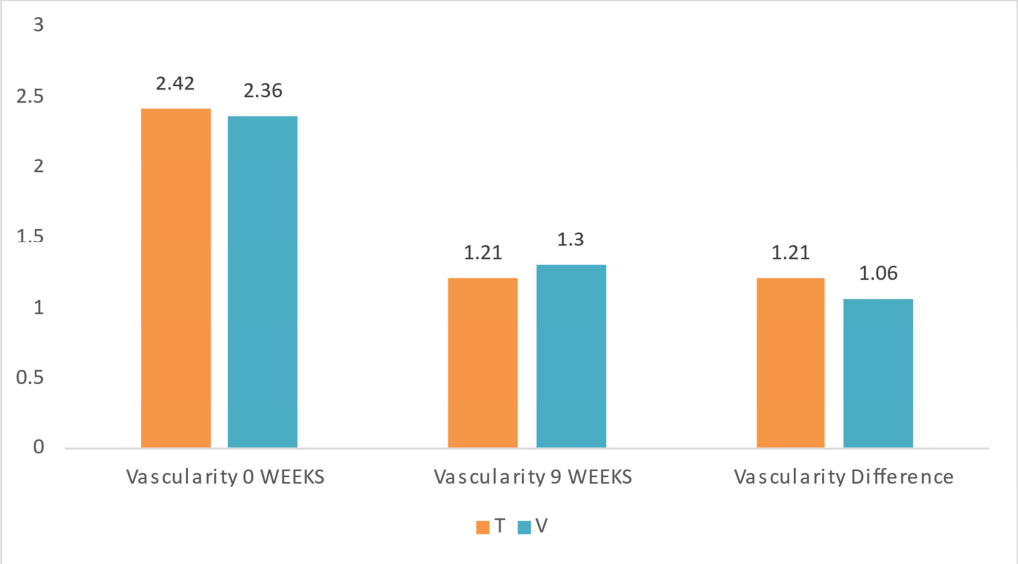


Figure 9: Bar diagram showing the vascularity scores of keloids among the study participants in the Triamcinolone and Verapamil group at 0 weeks and at the end of 9 weeks.

The median vascularity score for group T was 1, with an interquartile range (IQR) of 1 to 2, while for group V, the median vascularity score was also 1, but with a narrower IQR of 1 to 1. The sum of ranks for group T was 1176.5, whereas for group V, it was 1034.5. The statistical. analysis yielded a p-value. of 0.305., indicating no significant difference in vascularity between the two groups.

	Keloid group	Median (IQR)	Sum of ranks	P Value
Vascularity	T	1(1-2)	1176.5	0.305
	V	1(1-1)	1034.5	

Table 16: Shows the median, sum of ranks and p value obtained in the vascularity parameter of keloid.

The mean score of pigmentation was 2.18 in the Triamcinolone group at 0 weeks that is at baseline and the mean score of pigmentation in the Verapamil group was 2.15. At the end of 9 weeks, pigmentation score decreased to 1.33 in the Triamcinolone group and 1.33 in the Verapamil group, showing both the groups effective in reducing the pigmentation of keloids. Both the groups caused significant reduction in the pigmentation scores of keloids. There was no significant difference between both the groups in terms of pigmentation parameters.

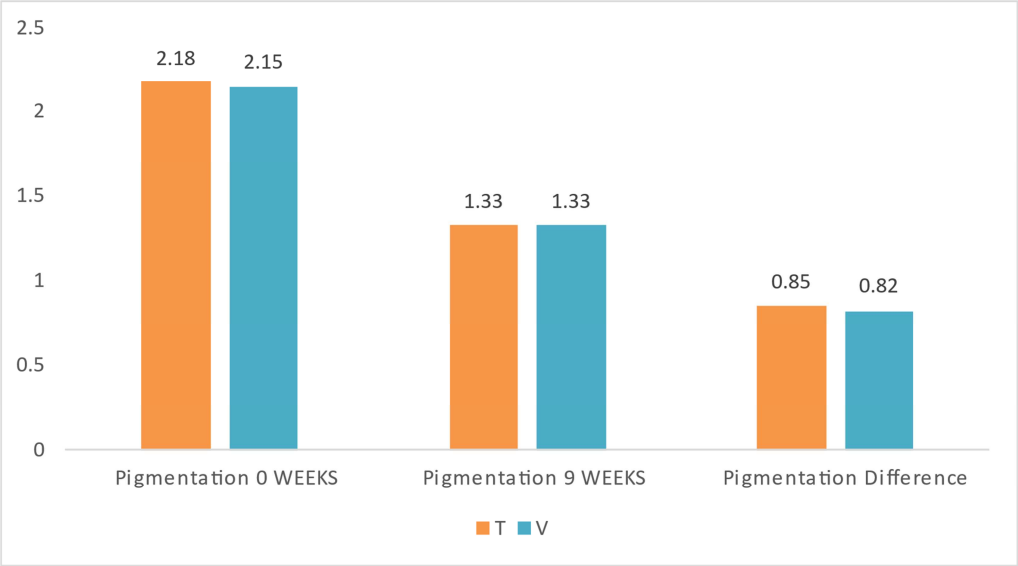


Figure 10: Bar diagram showing the pigmentation scores of keloids among the study participants in the Triamcinolone and Verapamil group at 0 weeks and at the end of 9 weeks.

	Keloid group	Median (IQR)	Sum of ranks	P Value
Pigmentation	T	1(1-1)	1118.5	0.827
	V	1(1-1)	1092.5	

Table 17: Shows the comparison of median, sum of ranks and p value obtained in the pigmentation parameter of keloid.

The median pigmentation score for both group T and group V was 1, with an interquartile range (IQR) of 1 to 1. The sum of ranks for group T was 1118.5, while for group V, it was 1092.5. The statistical analysis resulted in a p-value of 0.827, indicating no significant difference in pigmentation between the two groups.

The mean score of was 2.67 in the Triamcinolone group at 0 weeks that is at baseline and the mean score of pliability in the Verapamil group was 2.64. At the end of 9 weeks, pliability score decreased to 1.58 in the Triamcinolone group and 1.27 in the Verapamil group, showing both the groups effective in reducing the pliability of keloids. Both the groups caused significant reduction in pliability scores of keloids. There was no significant difference between both the groups in terms of pliability parameters.

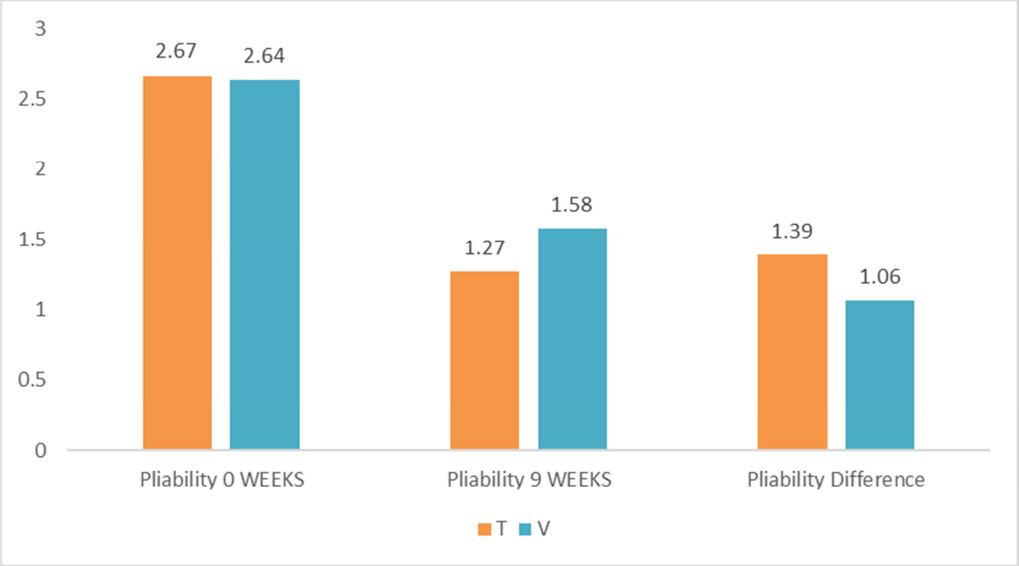


Figure 11: Bar diagram showing the pliability scores of keloids among the study participants in the Triamcinolone and Verapamil group at 0 weeks and at the end of 9 weeks.

	Keloid group	Median (IQR)	Sum of ranks	P Value
Pliability	T	1(1-2)	1229.5	0.081
	V	1(1-1)	981.5	

Table 18: Shows the comparison of median, sum of ranks and p value obtained in the pliability parameter of keloid.

The median. pliability score for parameter T was 1, with an interquartile range. (IQR) of 1 to 2, and a sum of ranks of 1,229.5, with a P-value of 0.081. For parameter V, the median pliability score was 1, with an IQR of 1 to 1, and a sum of ranks of 981.5. Since the p value. is not less than 0.05, there was no significant difference. between the two groups in terms of pliability.

The mean score of height was 2.18 in the Triamcinolone group at 0 weeks that is at baseline and the mean score of height in the Verapamil group was 2.39. At the end of 9 weeks, height score decreased to 1.06 in the Triamcinolone group and 1.67 in the Verapamil group, showing both the groups effective in reducing the height of keloids. Both the groups caused significant reduction in height scores of keloids. There was significant difference seen between both the groups in terms of height parameters, showing the Triamcinolone group causing more reduction in height as compared to Verapamil group.

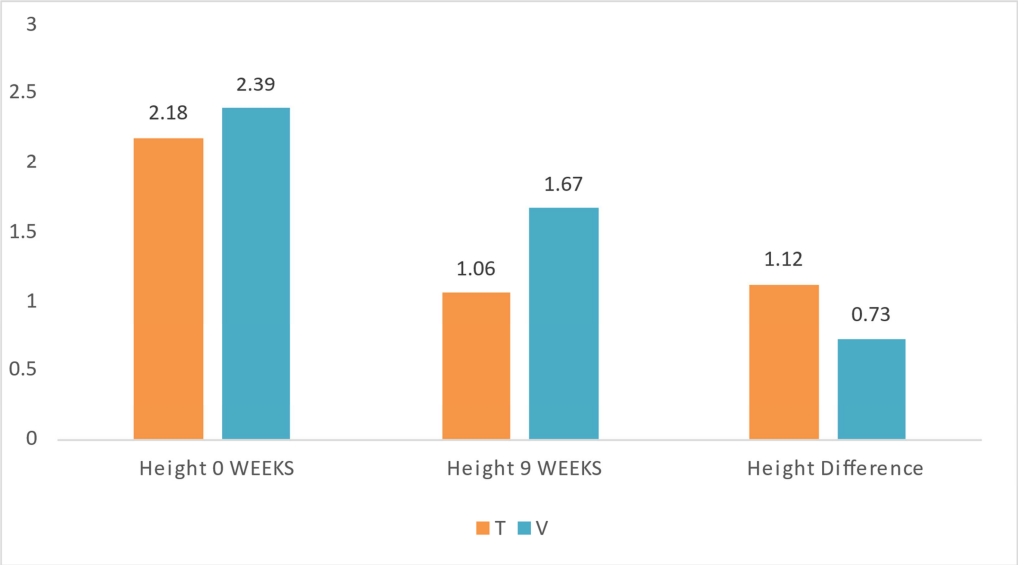


Figure 12: Bar diagram showing the height scores of keloids among the study participants in the Triamcinolone and Verapamil group at 0 weeks and at the end of 9 weeks.

The analysis comparing height measurements between two groups revealed intriguing findings. The keloid group exhibited a median height of **1 (IQR: 1-1)**, with a total sum of ranks reaching **1274.5**. In contrast, the control group had a median height of **1 (IQR: 0-1)** and a lower sum of ranks at **936.5**. Notably, the statistical comparison yielded a **P-value**. **of 0.009**, indicating a significant difference between the groups.

	Keloid group	Median (IQR)	Sum of ranks	P Value
Height	T	1(1-1)	1274.5	0.009*
	V	1(0-1)	936.5	

Table 19: Shows the comparison of median, sum of ranks and p value obtained in the height parameter of keloid.

The mean volume was 1.1 in the Triamcinolone group at 0 weeks that is at baseline and the mean of volume in the Verapamil group was 1.56. At the end of 9 weeks, volume decreased to 0.51 in the Triamcinolone group and 1.19 in the Verapamil group, showing both the groups effective in reducing the volume of keloids. Both the groups caused significant reduction in volume of keloids. There was significant difference seen between both the groups in terms of volume parameters, showing the Triamcinolone group causing more reduction in volume as compared to Verapamil group.

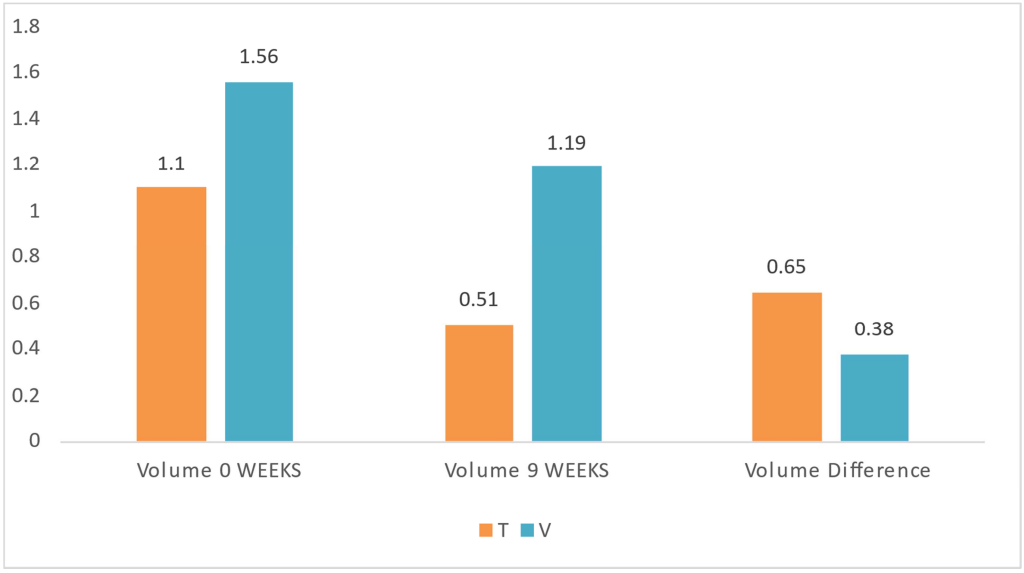


Figure 13: Bar diagram showing the volume of keloids among the study participants in the Triamcinolone and Verapamil group at 0 weeks and at the end of 9 weeks.

The median volume for group T was 0.36 (IQR: 0.12–0.92), with a sum of ranks of 1265.5. Meanwhile, group V had a median volume of 0.12 (IQR: 0.08–0.48), with a sum of ranks of 945.5. The P-value.for the comparison between the two groups was 0.04, indicating a statistically significant. difference.

	Keloid group	Median (IQR)	Sum of ranks	P Value
Volume	T	0.36(0.12-0.92)	1265.5	0.04*
	V	0.12(0.08-0.48)	945.5	

Table 20: Shows the comparison of median, sum of ranks and p value obtained in the volume parameter of keloid.

Visual analogue scale (patients' satisfaction) was also used for comparison between the two groups for analysis of effectiveness for the treatment of keloids.

Visual analogue scale (patients satisfaction)	0 weeks	9 weeks
1. Not satisfied (<25%)		
2. Slightly satisfied (25- 50%)		
3. Very satisfied (50- 75%)		
4. Extremely satisfied (75 – 100%)		

Table 21: Shows the Visual analogue scale (according to patients' satisfaction)

The Visual analogue scale score (according to patient satisfaction) was 1 in the Triamcinolone group at 0 weeks that is at baseline and that in the Verapamil group was also 1. At the end of 9 weeks, visual analogue scale score was improved to 3.3 in the Triamcinolone group and to 2.7 in the Verapamil group, showing both the groups effective for the treatment of keloids. Both the groups caused significant improvement of keloids in visual analogue scale. There was no significant difference seen between both the groups.

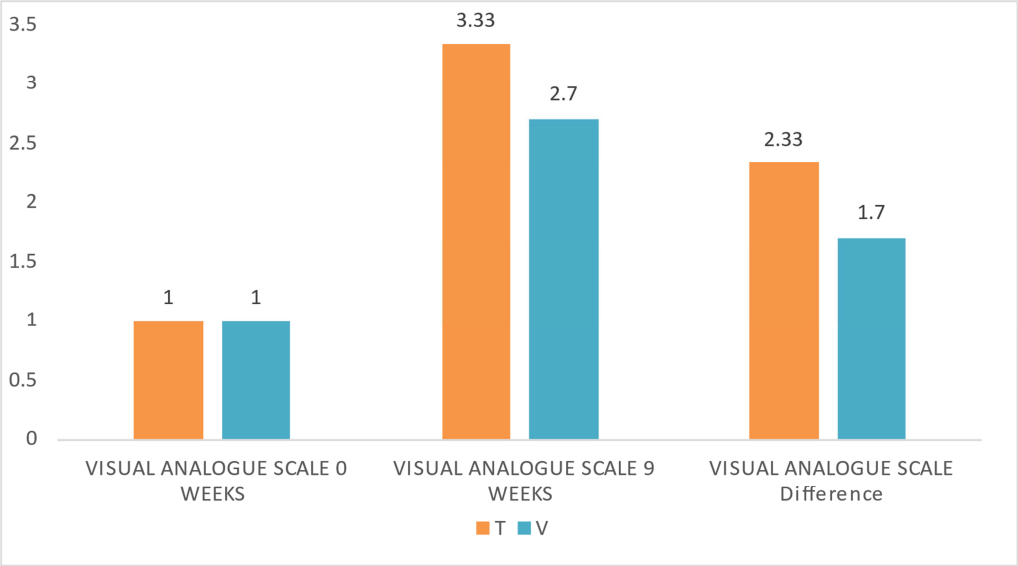


Figure 14: Bar diagram showing the visual analogue scale according to patient satisfaction of keloids among the study participants in the Triamcinolone and Verapamil group at 0 weeks and at the end of 9 weeks.

	Keloid group	Median (IQR)	Sum of ranks	P Value
VISUAL ANALOGUE SCALE	T	2(2-3)	1338.5	0.001*
	V	2(1-2)	872.5	

Table 22: Shows the comparison of median, sum of ranks and p value obtained in the two groups considering visual analogue scale of keloid.

The median Visual Analogue Scale (VAS) score for group T was 2 (IQR: 2–3), with a sum of ranks of 1338.5. In contrast, group V had a median VAS score of 2 (IQR: 1–2), with a sum of ranks of 872.5. The P-value for the comparison between the two groups was 0.001, indicating a statistically significant difference.

Numeric pain rating scale was used to find out the residual burning pain associated with keloids and to see how effective the treatment was in reducing it by calculation the numeric pain rating score at the end of 9 weeks.

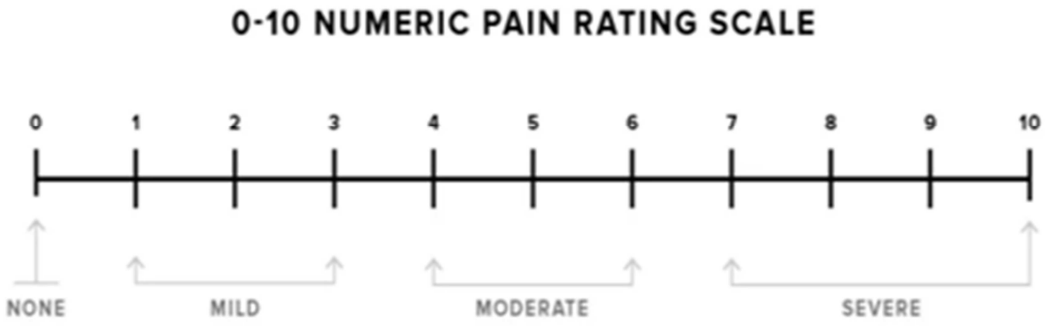


Figure 15: Shows the Numeric pain rating scale.

The Numeric pain rating score was 2.33 in the Triamcinolone group at 0 weeks that is at baseline and that in the Verapamil group was 2.27. At the end of 9 weeks, score was reduced to 0.21 in the Triamcinolone group and to 1.24 in the Verapamil group, showing both the groups effective for reducing the burning pain associated with keloids. There was significant difference seen between both the groups for treating the pain associated with keloids, showing triamcinolone group being more effective as compared to verapamil group.

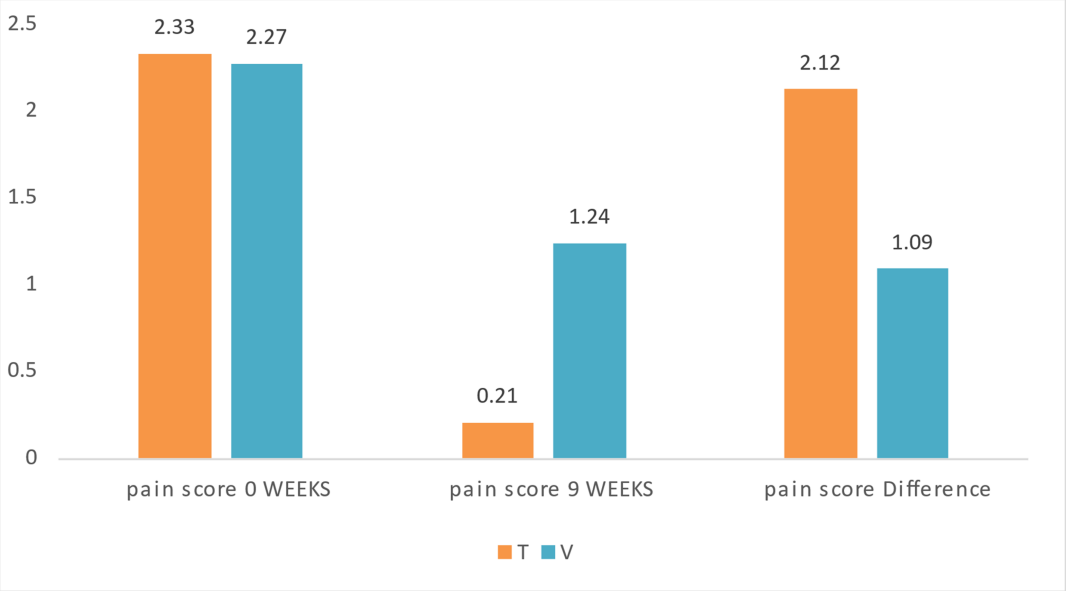


Figure 16: Bar diagram showing the Numeric pain rating score of keloids among the study participants in the Triamcinolone and Verapamil group at 0 weeks and at the end of 9 weeks.

	Keloid group	Median (IQR)	Sum of ranks	P Value
pain score	T	2(2-3)	1435	<0.001*
	V	1(1-1)	776	

Table 23: Shows the comparison of median, sum of ranks and p value obtained in the two groups considering Numeric pain rating score of keloids.

In the keloid group, the pain score varied significantly between the two groups. Group T had a median pain score of 2 (IQR: 2–3), with a sum of ranks of 1435. In contrast, group V had a lower median pain score of 1 (IQR: 1–1), with a sum of ranks of 776. The P-value for this comparison was less than 0.001, indicating a highly statistically significant difference between the two groups.

VAS pruritis scoring was used to find out the pruritis associated with keloids and to see how effective the treatment was in reducing it by calculation the VAS pruritis score at the end of 9 weeks.

VAS scoring	Meaning
0 points	No pruritus
>0 points but <4 points	Mild pruritus
≥4 points but <7 points	Moderate pruritus
≥7 points but <9 points	Severe pruritus
≥9 points	Very severe pruritus

Figure 17: Shows VAS pruritis score for keloids.

The VAS pruritis score was 2.03 in the Triamcinolone group at 0 weeks that is at baseline and that in the Verapamil group was 2.03. At the end of 9 weeks, score was reduced to 1.03 in the Triamcinolone group and to 1.03 in the Verapamil group, showing both the groups effective for reducing the pruritis associated with keloids. There was no significant difference seen between both the groups for treating the pruritis associated with keloids, showing triamcinolone group and verapamil group equally effective in reducing the pruritis associated with keloids.

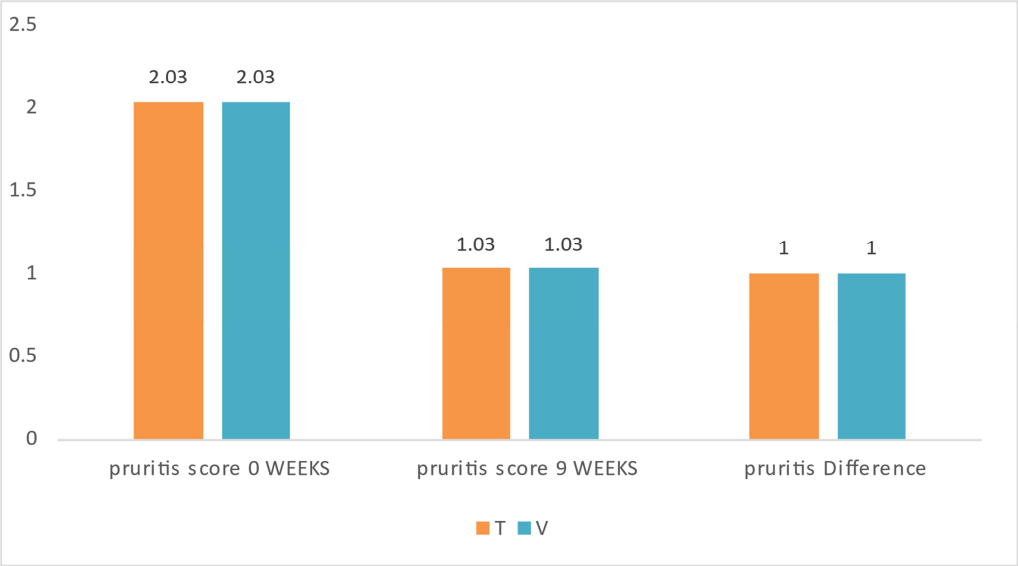


Figure 18: Bar diagram showing the VAS pruritis score of keloids among the study participants in the Triamcinolone and Verapamil group at 0 weeks and at the end of 9 weeks.

The median (interquartile range, IQR) for pruritus was 1 (1–1) for both treatment (T) and control (V) groups. The sum of ranks for both groups was 1105.5. The P-value. for the comparison was 1, indicating no statistically significant difference. between the two groups in terms of pruritus.

	Keloid group	Median (IQR)	Sum of ranks	P Value
pruritis	T	1(1-1)	1105.5	1
	V	1(1-1)	1105.5	

Table 24: Shows the comparison of median, sum of ranks and p value obtained in the two groups considering VAS pruritis score for pruritis associated with keloids.

In analysing the side effects associated with the two treatment modalities for keloids, the numeric pain rating score was assessed during the injection of Triamcinolone and Verapamil. The results revealed that the Triamcinolone group had a mean pain score of 5.39, while the Verapamil group reported a higher mean pain score of 7.79. This indicates that intralesional Verapamil injections are significantly more painful compared to intralesional Triamcinolone, highlighting a notable difference in patient discomfort between the two treatments.

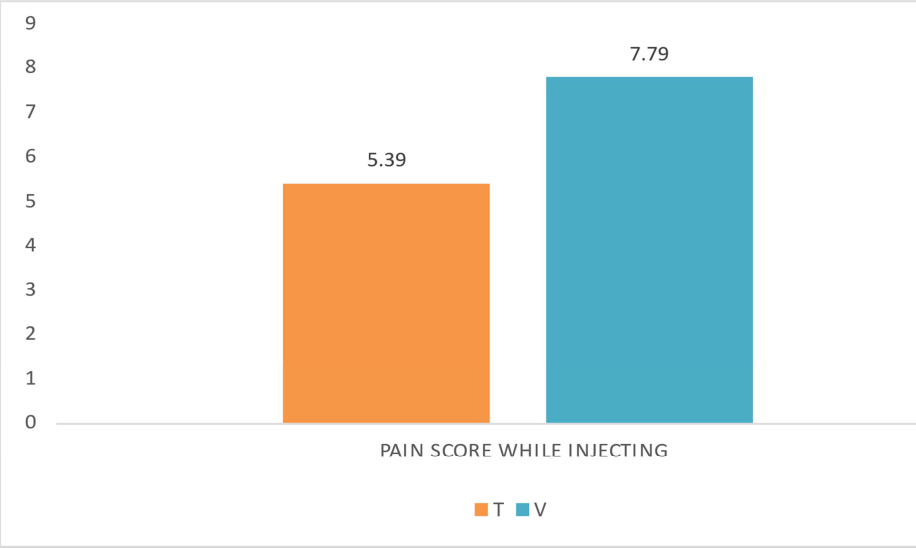


Figure 19: Bar diagram showing the Numeric pain rating score while injecting intralesional Triamcinolone and Verapamil.

	Keloid group	Median (IQR)	Sum of ranks	P Value
PAIN SCORE WHILE INJECTING	T	5(5-6)	593	<0.001*
	V	8(8-8)	1618	

Table 25: Shows the comparison of the pain scores while injecting triamcinolone and Verapamil.

The table presents the pain scores experienced while injecting two different treatments—Triamcinolone (T) and Verapamil (V)—in patients with keloids.

- **Median (Interquartile Range, IQR):**
  - The median pain score for the **Triamcinolone (T) group** was **5**, with an interquartile range. (IQR) . of **5–6**.
  - The median pain score for the **Verapamil (V) group** was **8**, with a very narrow IQR of **8–8**, indicating less variability in pain perception among patients receiving Verapamil.
- **Sum of Ranks:**
  - The **Triamcinolone group** had a sum of ranks of **593**, suggesting lower overall pain rankings among participants.
  - The **Verapamil group** had a significantly higher sum of ranks, **1618**, reinforcing that most patients experienced higher pain levels with this treatment.
- P- value:

  The P-value.is **less than 0.001**, which is statistically significant. This indicates a strong difference between the pain scores of the two treatment groups, with Verapamil causing significantly more pain than Triamcinolone during injection.

Interpretation: Patients receiving **intralesional Verapamil** injections experienced **substantially greater pain** compared to those receiving **intralesional Triamcinolone**. The statistical significance of the P-value confirms that this difference is unlikely due to chance, making it a key consideration when selecting treatment modalities for keloids.

	Keloid group	Median (IQR)	Sum of ranks	P Value
Vascularity	T	1(1-2)	1176.5	0.305
	V	1(1-1)	1034.5	
Pigmentation	T	1(1-1)	1118.5	0.827
	V	1(1-1)	1092.5	
Pliability	T	1(1-2)	1229.5	0.081
	V	1(1-1)	981.5	
Height	T	1(1-1)	1274.5	0.009*
	V	1(0-1)	936.5	
Volume	T	0.36(0.12-0.92)	1265.5	0.04*
	V	0.12(0.08-0.48)	945.5	
VISUAL ANALOGUE SCALE	T	2(2-3)	1338.5	0.001*
	V	2(1-2)	872.5	
pain score	T	2(2-3)	1435	<0.001*
	V	1(1-1)	776	
pruritis	T	1(1-1)	1105.5	1
	V	1(1-1)	1105.5	
PAIN SCORE WHILE INJECTING	T	5(5-6)	593	<0.001*
	V	8(8-8)	1618	

*Significant

Mann Whitney U T

Table 26: Shows the comparison of various parameters used and the p- value obtained.

Side effects	Triamcinolone group	Verapamil group
1.Hypopigmentation	11	0
2. Atrophy	9	0
3. Telangiectasia	6	0
4. Hypotension	0	0
5. Dizziness	0	0
6. Anaphylaxis	0	0

Table 27: Shows the side effects of both the intralesional therapy at the end of 9 weeks.

1. **Triamcinolone was associated with a significant risk of skin-related side effects:**
    - **Hypopigmentation (33.3%)**, **atrophy (27.3%)**, and **telangiectasia (18.2%)** were all observed in this group. Triamcinolone group causing hypopigmentation in one-third of the patients
    - These side effects may be concerning for patients who prioritize skin appearance.
2. **Verapamil showed no recorded side effects** in this study.
    - Despite being **more painful during injection**, it did not cause skin thinning, discoloration, or vascular changes.
    - This makes Verapamil a potentially safer alternative in terms of long-term skin integrity.

3. **Neither treatment caused systemic side effects** such as **hypotension, dizziness, or anaphylaxis**.
    - This suggests that both medications are **safe from a systemic health perspective**

While **Triamcinolone is effective**, it carries a higher risk of **localized skin changes**, which may impact patient satisfaction. **Verapamil, though more painful during administration, had no recorded side effects**, making it a preferable option for patients concerned about aesthetic outcomes.

Thus, the choice between these two treatments should consider **both efficacy and patient tolerance**, balancing **pain levels vs. cosmetic side effects**.

DISCUSSION

The comparison between intralesional triamcinolone acetonide and intralesional verapamil hydrochloride has been done by many authors. Various scores have been used for comparison, but the comparison between the pain and pruritis scores has been done by very few. There are many randomized control trials and meta-analysis, but in our study both the intralesional therapy is done in the same patient making the groups completely comparable in terms of age and sex and avoiding bias. There are no studies with such comparison.

This study is an attempt to compare the effectiveness and side effects of triamcinolone acetonide and verapamil chloride in the same with patient with two keloids.

It is a hospital based interventional study carried out on a total of 33 patients over a span of one year.

Age group

	Our study	**Margaret et al**(78)	**Belie et al**(79)	**Zahra et al**(80)
Age groups	18- 70 years	10 -50 years	>18 years	18 and 50 years
Mean age in Triamcinolone group	35.3	20 years	Not mentioned	36.09 years
Mean age in verapamil group	35.3	26 years	Not mentioned	36.09 years

Table 28: Shows the comparison of different age groups kept in studies compared.[75–77]

Aetiology of keloids

<table>
<tr><th>Our study</th><th>Margaret et al (78)</th><th>Belie et al (79)</th></tr>
<tr>
<td>Etiology in each group Triamcinolone and Verapamil (n=33)

1. Surgery – 27.2%
2. Acne – 27.2.%
3. Unknown-18.18%s
4. Trauma- 12.12%
5. Shaving - 12.12%
6. Radiotherapy-3.03%</td>
<td>
<table>
<tr><th></th><th>Triamcinolone group (n=27)</th><th>Verapamil group (n=27)</th></tr>
<tr><td>Pimple</td><td>9</td><td>9</td></tr>
<tr><td>Ear piercing</td><td>7</td><td>4</td></tr>
<tr><td>Road traffic accident</td><td>7</td><td>11</td></tr>
<tr><td>Surgery</td><td>4</td><td>2</td></tr>
<tr><td>Post-vaccination</td><td>0</td><td>1</td></tr>
</table>
</td>
<td>Etiology in each group Triamcinolone and Verapamil(n=16)
1. Barbing / Shaving- 13, 17%
2. Trauma -21, 27%
3. Acne- 13, 17%
4. Piercing 11-14%
5. Boil - 6- 8%
6. Tattoo -5,6%
7. Burns- 3-4%
8. Vaccination, 3-4%
9. Surgery- 1- 1%
10. Unknown- 1-1%
11. Heat Rashes- 1,1%</td>
</tr>
</table>

Table 29: Shows the comparison of different aetiology of keloids kept in studies compared.

Location of keloids

Our study	**Margaret et al** [78]	**Belie et al** [79]
1.Anterior chest- 57.58% 2.Upper arm -21.21% 3.Dorsum of hand-6.06% 4.Breast- 6.06% 5.Scapula- 3.03% 5.Lower arm – 3.03%	Table 2: Location of scars in each study group Face/Neck 2 4 Ear lobe 7 2 Sternum 8 4 Abdomen/Chest 2 4 Upper limb 5 10 Lower limb 2 3	Triamcinolone group- 1. 243.8% - head and neck 2. 37.5% - trunk 3. 18.8% in the upper limb. Verapamil group- 1.37% -head and neck 2.48.1% - trunk 3.11.1% - upper limb 4. 3.7% - lower limb.

Table 30: Shows the comparison of different location of keloids in different studies.

Type of study and methodology

Our study	Margaret et al [78]	Belie et al [79]	Zahra et al[80]
Non randomized, interventional. study	Randomized. control trial, parallel and single blinded study.	Randomized. control study, single blind.	Randomized control study, single blind.
Intralesional TAC and verapamil was given at 1. 0 weeks (first session) photographs were taken 2. 3 weeks (second session) 3. 6 weeks (third session) 4. 9 weeks – photographs taken	Intralesional TAC and verapamil was given every 3 weeks till the scar flattened, till 6 months at least. Next follow up was done at the end of one year.	Intralesional TAC and verapamil was given every 2 weeks, maximum of 6 doses were given.	Intralesional TAC and verapamil was given every 3 weeks with 3 monthly follow up.

Table 31: Shows the type of study and methodology used.

Sample of study

Our study	Margaret et al [78]	Belie et al [79]	Zahra et al [80]
33 patients with more than equal to two keloids.	54 patients in each group.	27 patients in each. group.	16 patients in each. group.

Table 32: Shows the different sample size used in the studies compared to our study.

Parameters measured

Our study	Margaret et al[78]	Belie et al[79]	Zahra et al[80]
1.Vancouver Scar Scale(VSS) consist of four parameters - height, vascularity, pliability and pigmentation. Height of keloids is accurately measured with a ruler in millimeters. Scar vascularity. and pigmentation. will be assessed by visual inspection. Scar pliability. is subjectively assessed by palpation	**1.Vancouver Scar Scale**	**1.The pruritus scale score** No itching- 1 Itching present, but does not affect daily. activities- 2 Itching present, bothers me, affects my. concentration- 3 Itching present, cannot go about normal business- 4 Itching present, worse, prevent from sleeping -5	**1.Vancouver Scar Scale**
2.Visual analogue scale		**2.Width, length, and height of keloids by ruler scale.**	**3.Width, length, and height of keloids by vernier calliper.**
3.VAS pruritis score			
4.Numeric pain score			
5.Volume by measuring the length, breadth and height of keloids by ruler scale.			

Table 33: Shows the different parameters used in the studies compared to our study.

Statistical analysis comparison and p value used-

Statistical analysis was done by Mann Whitney.U test with significant p value being <= 0.5. Margaret et al used Kaplan Meier graphs and log rank test to compare different parameters with significant p value being <= 0.5. (78) Whereas, Belie et al did the data analysis using Statistical Package for Social Science (SPSS). version 20 significant p value being <= 0.5.(79) Zahra et al also considered p value <= 0.05 being significant.[80]

Comparison of different results of studies with our study

- In our study there was significant.difference.among the height and volume parameters of VSS scale in triamcinolone group as compared to the verapamil group (p. value <= 0.05). There was no significant difference seen in vascularity, pigmentation, pliability and pruritis score between both the groups. There was significant difference in the visual analogue scale and pain score associated with keloids in triamcinolone group as compared to verapamil group. There was also significant difference seen in the pain score while injecting, with verapamil having more pain while injecting.
- Study by Margaret et al showed that the time taken for the reduction of vascularity, pliability and height was less in the triamcinolone group as compared to the verapamil group with significant difference seen in these parameters. The time taken for reduction of length between the two groups was not significant.[78] The time taken for reduction of width and height parameter was also not found to be significant. They didn't compare the pruritis and pain parameters as it was done in our study. But this study

compared the time taken for reduction of parameters which our study did not include.

- Study by Belie et at showed that there was no significant difference seen in length parameters of keloids between the Triamcinolone and Verapamil group. There was a significant.difference seen in the width between the two groups.[(79)] They did not compare the height and volume parameter.

  Where as in our study there was comparison of all the length, height and breath between the two groups and comparison of volume which showed significant difference between the two groups.

- Study of Belie et al showed that there was improvement in the pain score immediately after 7 days of first injection of Triamcinolone, whereas the pain score in the Verapamil group reduced after 28 days after its first dose. [(79)] There was a statistically significant. difference present in pain scores reduction between the two groups (p value <= 0.05).[(79)]Triamcinolone group had more effect in reducing the pain associated with keloids as compared to the pruritis associated with keloids. The study also showed that there was significant difference between the two group in reducing the pruritis associated with keloids. There was complete resolution of pruritis at the end of fourteenth week in triamcinolone group as compared to pain which completely resolved in the sixth week. There was more improvement in the pruritis associated with keloids of the trunk region as compared to those present in lower limbs.

- Zahra et al showed significant improvement in the length, width, flexibility in both the groups with p. value being <= 0.05. This study didn't measure the pain and pruritis scores between the two groups like in our study. [(80)]

Our study	Margaret et al[78]	Belie et al[79]	Zahra et al[80]
Triamcinolone group had more side effects as compared to Verapamil group. In our study 11 patients out of 33 patients suffered from hypopigmentation in the Triamcinolone group and 9 patients had atrophy and 6 patients had telangiectasia. Whereas none such side effects were observed in Verapamil group. Numeric pain score was also calculated while injecting and it was found that the Triamcinolone group had 5.39 whereas the Verapamil group had 7.79, a higher pain score while injecting it as compared to Triamcinolone. Side effects mentioned in other studies such as insomnia , hypotension was not seen in any of the patients of Verapamil group.	In triamcinolone group the side effects observed were increased profuse sweating, hypopigmentation and irregular menstrual Cycles, but none such side effects were observed in Verapamil group.	The side effects seen in the Verapamil group were insomnia and headache seen in 5.3% of the total number. of patients. In Triamcinolone group Thirty- two patients had hypopigmentation and thirty patients had skin atrophy and two patients had ulceration.	Three patients in the Verapamil group complained of side effects as compare to the seven patients in Triamcinolone group. Verapamil group patient had headache 6.2%. (n = 1), atrophy 6.2%. (n = 1), and insomnia 6.2%. (n = 1). Triamcinolone group had more side effects like atrophy 25% (n = 4), hypopigmentation 12.5% (n = 2) and ulceration of the keloid 6.2% (n = 1).

Table 34: Shows the different side effects of the TAC and Verapamil group in our study vs those found in other studies.

CONCLUSION

This study shows that both intralesional TAC and verapamil hydrochloride, both are effective in reducing the height, volume, vascularity, pigmentation and pliability of keloids.

TAC causes more reduction in the volume and height of keloids as compared to verapamil.

Verapamil is more effective in reducing the vascularity of keloids as compared to other parameters such as height, volume, pigmentation and pliability.

Both the modalities can be used effectively used for the treatment of keloids and giving good results.

Side effects of intralesional TAC is more as compared to intralesional Verapamil. Side effects of intralesional TAC include hypopigmentation. Atrophy and telangiectasia. None such side effects are observed in the Verapamil group. Side effects of hypotension and dizziness was not observed after giving intralesional Verapamil.

Anaphylaxis was not observed in any of the groups post intralesional therapy. Intralesional Verapamil is more painful as compared to intralesional TAC.

Both TAC and Verapamil are effective in reducing the subjective symptoms associated with keloid such as burning pain and pruritis. Intralesional TAC is more effective in reducing the burning pain associated with keloids as compared to intralesional Verapamil. Both the modalities are effective in reducing the pruritis associated with keloids.

So intralesional Verapamil can be used as effective modality with better cosmetic results as compared to intralesional TAC. Can also be used for patients with uncontrolled diabetes. Can be used for treatment of keloids that developed atrophy, telangiectasia and hypopigmentation post intralesional TAC therapy. But since the intralesional therapy is painful, the choice also depends on the pain perception of individual to the therapy. Also, intralesional verapamil therapy is cheaper than intralesional TAC, serves as a cot effective treatment.

SUMMARY

- The mean age of the patients recruited was 37.24 years.
- 24 were males, making up 72.73% of the sample population, while 9 were females, accounting for 27.27%
- The most common aetiologies were surgery and acne, each accounting for 27.2% of the participants. This was closely followed by cases with unknown aetiology, which made up 18.18%. Trauma and shaving were identified as the second least common causes, each contributing to 12.12% of the cases. The least frequent cause was radiotherapy, which was responsible for just 3.03% of the participants.

- The majority of keloids in this study were located on the anterior chest**,** affecting 57.58% of cases. The upper arm was the second most common site, accounting for 21.21%**.** Other locations included the breast and dorsum of the hand**,** each making up 6.06% of cases. Less frequently, keloids were found on the arm, back, and scapular region**,** with each of these sites representing 3.03% of occurrences.

- The statistical analysis yielded a p-value of 0.305, indicating no significant difference in vascularity between the two groups.
- The statistical analysis resulted in a p-value of 0.827, indicating no significant difference in pigmentation between the two groups.
- Since the p-value is not less than 0.05, there was no significant difference between the two groups in terms of pliability.
- The p-value for the comparison between the two groups was 0.04, indicating a statistically significant difference in volume.

- The statistical comparison yielded a p-value of 0.009**,** indicating a significant difference between the groups in height.
- The p-value for the comparison between the two groups was 0.001, indicating a statistically significant difference in Visual analogue scale.
- The p-value for this comparison was less than 0.001, indicating a highly statistically significant difference between the two groups in the pain score.
- The p-value for the comparison was 1, indicating no statistically significant difference between the two groups in terms of pruritus.
- The P-value. is less than 0.001, which is statistically significant. This indicates a strong difference between the pain scores of the two treatment groups, with Verapamil causing significantly more pain than Triamcinolone during injection.
- Triamcinolone was associated with a significant risk of skin-related side effects: Hypopigmentation (33.3%), atrophy (27.3%), and telangiectasia (18.2%) were all observed in this group.
- Verapamil showed no recorded side effects in this study. Despite being more painful during injection, it did not cause skin thinning, discoloration, or vascular changes.

STRENGHTS

- Our study is a non-biased study, comparison of both intralesional triamcinolone and verapamil done on the same patient making it identical and comparable in age and sex.
- No Indian studies comparing the pruritis and pain parameters associated with keloids.
- We have used many scoring scales to measure the effectiveness of intralesional therapy for keloids whereas other studies have only used the VSS scale.

LIMITATIONS

Our study faces a few limitations that require attention.

- Firstly, the sample size employed in our research is relatively small. This raises concerns regarding the representativeness of our findings to the broader population. Increasing the sample size could enhance the robustness and generalizability of our results.
- Secondly, the follow-up period in our study is limited. This restricts our ability to observe any potential long-term effects or changes. Extending the follow-up period would allow for a more comprehensive understanding of the dynamics at play.
- Thirdly, the duration of our study is relatively short. This temporal constraint may have implications for capturing all relevant variations or trends pertaining to the phenomenon under study. Extending the study period could provide a more nuanced perspective on the subject matter.

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ANNEXURE – I - INFORMED CONSENT FORM

Title of the study: "an interventional study comparing intralesional verapamil and intralesional triamcinolone acetonide in the treatment of keloids in a tertiary care hospital" attending KLE's Dr. Prabhakar Kore Hospital and MRC, Belagavi.

NAME OF STUDENT/PRIMARY INVESTIGATOR:

Department of Dermatology, Venereology and leprosy

Ladies Can hostel

Jawaharlal Nehru Medical College KAHER University

Belagavi-590010 Karnataka

NAME OF GUIDE/ CO-INVESTIGATOR

Associate professor

Department of Dermatology, Venereology and leprosy

Jawaharlal Nehru Medical College KAHER University

Belagavi-590010 Karnataka

OBJECTIVE: Primary objective: To assess and compare the efficacy of two treatment options: intralesional verapamil hydrochloride and triamcinolone acetonide in treatment of keloid in patient aged 18 to 70 years.

Secondary objective: To assess and compare the safety of two treatment options: intralesional verapamil hydrochloride and triamcinolone acetonide in treatment of keloid in patient aged 18 to 70 years

INTRODUCTION: Keloids is an abnormal fibrous tissue formed at site of injury. It causes lot of distress, pain, itching and disfigurement to the patients. So, this study is done to compare a new treatment modality that is injection verapamil with injection triamcinolone acetonide for the treatment of keloids. So, this injection verapamil can serve as a new treatment modality in future for the treatment of keloids. People who have given the consent and fit into this study criteria will have benefits of this study like reduction in the size and color of the keloids. But some of them can have side effects like pain at the site while giving injection or the lesion can become red and have infection at the site.

EXPLANATION OF PROCEDURE: Patient who fit into the study criteria and who have given consent for the study are taken. Before starting treatment, a detailed history, clinical examination is done. Digital photographs of Two keloids are taken using identical camera settings and room lighting at baseline first before giving injection and at the end of 16 weeks. Vancouver scar scoring of acne scars will be done. Precautions before and after the procedure will be advised to the patient. Two Keloids are selected. The mentioned scale scores the scars on 4 parameters: height, vascularity, pliability, and pigmentation. Height of keloids is accurately measured with a ruler in millimeters. Scar vascularity and pigmentation is assessed by visual inspection. Scar pliability is subjectively assessed by palpation. First keloid is given

intralesional triamcinolone acetonide and second keloid is given intralesional verapamil. The injections are given with the help of insulin syringe. Vial of TAC having 40mg/ ml is taken and is diluted with lignocaine. First keloid will receive intralesional triamcinolone acetonide, maximum of 1ml is given, every 3 weeks for 9 weeks (3 sessions). Second keloid receives intralesional verapamil hydrochloride (2.5 mg/ ml)1ml every 3 weeks for 9 weeks (3 sessions). Scoring is done one before the first injection and other after 9 weeks by Vancouver scar scale (VSS), Visual analogue scale, VAS pruritis scale, numeric pain rating scale while injecting as well as the residual pain associated with keloids. Reduction in the keloid height, changes in the color is compared between two treatment modalities. Patient is also explained about the side effects of the injections like pain while injecting, redness and infection at the site. Benefits is also explained like reduction in the height and color of keloids at the end of treatment.

WITHDRAWAL FROM PARTICIPATION IN THE STUDY: Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

POSSIBLE BENEFITS FROM PARTICIPATING IN THE STUDY: You will have benefits by participating in this study like reduction in size and colour of keloids. The data gathered will help the population at large.

POSSIBLE RISKS FROM PARTICIPATING IN THE STUDY: There are some risks involved in participating in this study like pain while injecting, redness and infection at the site.

PRIVACY AND CONFIDENTIALITY: The information collected from you will be coded, to prevent any person from identifying you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

FINANCIAL INCENTIVES: You will not receive any payment for participating in this study.

AUTHORIZATION FOR PUBLICATION OF AGGREGATED DATA: Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups. However, your identity will never be revealed.

QUESTIONS: In case of any questions with regard to this study, you are free to contact: Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

LEGAL RIGHTS: By signing this consent form, we are not waving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision to participate in the study "**AN INTERVENTIONAL STUDY COMPARING INTRALESIONAL VERAPAMIL AND INTRALESIONAL TRIAMCINOLONE ACETONIDE IN THE TREATMENT OF KELOIDS IN A TERTIARY CARE HOSPITAL"**. My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator

ANNEXURE II - PROFORMA

TITLE: A comparative study between intralesional verapamil and intralesional triamcinolone in the treatment of keloids in a tertiary care hospital.

Demographic details			
Name		Marital status	
Age		Gender	
Occupation		Case number	
Address	Urban	Op number	
Contact no.		Ip number	

Pregnant: Yes [ ] No [ ] Lactation: Yes [ ] No [ ]

1. Diagnosis_____

2. Chief complaints_____

Duration of Keloids: _____

Cause for Keloids: _____

Site of keloids: _____

3.Associated Symptoms

Symptom	Present	Absent
Pruritis	[ ]	[ ]
Pain	[ ]	[ ]
Discharge	[ ]	[ ]

Type of discharge: _____

4.History of Treatment Taken

Treatment Type	Present	Absent
Systemic	[ ]	[ ]
Topical	[ ]	[ ]
Intralesional	[ ]	[ ]
Other	[ ]	[ ]

Mention details (if any): _____

5.Past History

History Type	Present	Absent
Surgery	[ ]	[ ]
Infections	[ ]	[ ]
Trauma at keloid site	[ ]	[ ]
Occurred spontaneously	[ ]	[ ]
Diabetes Mellitus (DM)	[ ]	[ ]
Hypertension (HTN)	[ ]	[ ]

Any other comorbidities: _____

Family History of Keloids: Present [ ] Absent [ ]

6.Personal History

Diet: Mixed [ ] Veg [ ]

7.Menstrual & Obstetric History

Menstrual History	Regular [ ]	Irregular [ ]
Type of Delivery	Vaginal [ ]	Caesarean [ ]
If Caesarean	Classic [ ]	LSCS [ ]

8.General Physical Examination

1) Weight: _____ Kg

2) Height: _____ cm

3) BMI: _____

Local Examination

Examination Type	Present	Absent
Erythema	[ ]	[ ]
Tenderness	[ ]	[ ]
Number and Site of Keloid	_____	
Colour	_____	
Size	_____	

Other findings (if any): _____

Procedure explained to patient: Digital photographs of Two keloids are taken using identical camera settings and room lighting at baseline first before giving injection and at the end of 16 weeks. Vancouver scar scoring of acne scars will be done. Precautions before and after the procedure will be advised to the patient. Two Keloids will be randomly selected. The mentioned scale scores the scars on 4 parameters: height, vascularity, pliability, and pigmentation. Height of keloids is accurately measured with a ruler in millimeters. Scar vascularity and pigmentation is assessed by visual inspection. Scar pliability is subjectively assessed by palpation. First keloid is given intralesional triamcinolone acetonide and second keloid is given intralesional verapamil. The injections are given with the help of insulin syringe. Vial of TAC having 40mg/ ml is taken and is diluted with lignocaine. First keloid will

receive intralesional triamcinolone acetonide, maximum of 1ml is given, every 3 weeks for 9 weeks (3 sessions). Second keloid receives intralesional verapamil hydrochloride (2.5 mg/ ml)1ml every 3 weeks for 9 weeks (3 sessions). Scoring is done one before the first injection and other at 9 weeks by Vancouver scar scale (VSS), Visual analogue scale, VAS pruritis scale, numeric pain rating scale while injecting as well as the residual pain associated with keloids. Safety and efficacy are measured.

Volume (ruler scale):

Length: Breadth: Height: Volume: (Lengthx Breadthx Height)

Vancouver scar scale:

VANCOUVER SCAR SCALE	SCAR CHARACTERISTIC	SCORE
VASCULARITY	NORMAL	0
	PINK	1
	RED	2
	PURPLE	3
PIGMENTATION	NORMAL	0
	HYPOPIGMENTATION	1
	HYPERPIGMENTATION	2
PLIABILITY	NORMAL	0
	SUPPLE	1
	YIELDING	2
	FIRM	3

	ROPES	4
	CONTRACTURES	5
HEIGHT (mm)	FLAT	0
	<2	1
	2-5	2
	>5	3

Visual Analogue scale

Visual Analogue Scale (Patients' Satisfaction)

Satisfaction Level	**0 Weeks**	**9 Weeks**
1. Not satisfied (<25%)		
2. Slightly satisfied (25-50%)		
3. Very satisfied (50-75%)		
4. Extremely satisfied (75-100%)		

Numeric pain rating scale while injecting as we well as the residual pain before injecting:

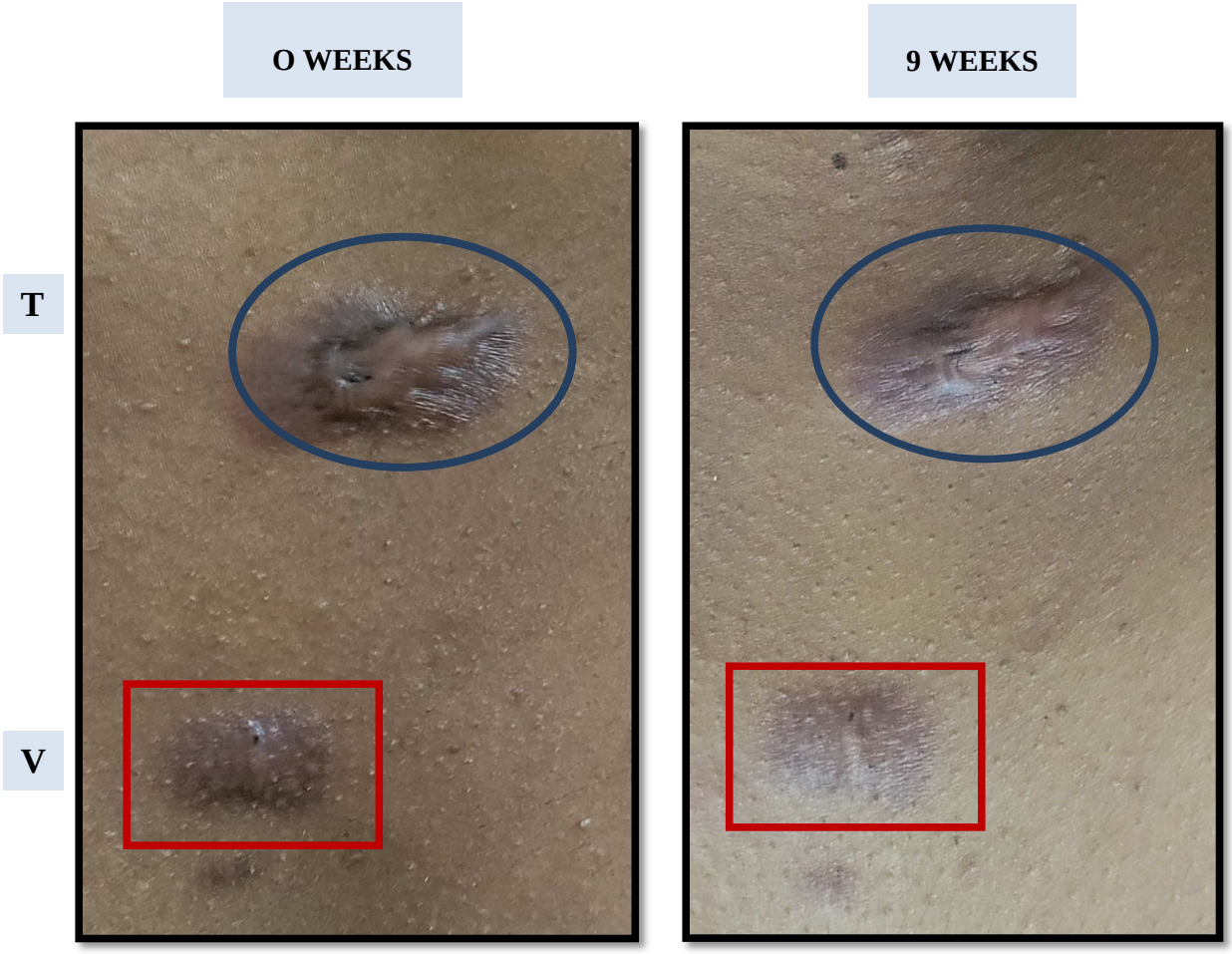
0-10 Numeric Pain Rating Scale

Pain Score	Pain Level
0	None
1-3	Mild
4-6	Moderate
7-10	Severe

VAS pruritis score:

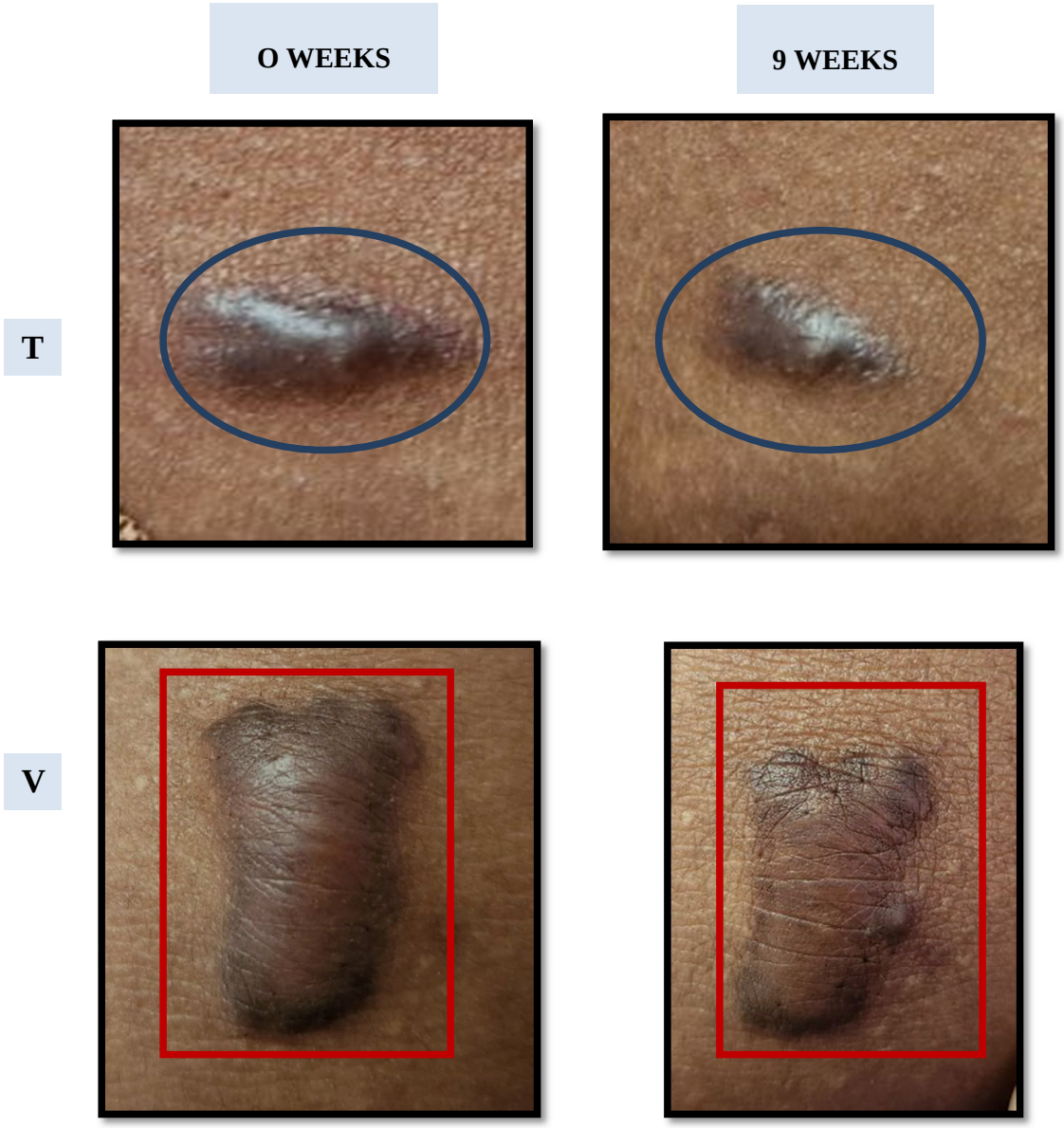
VAS Scoring	Meaning
0 points	No pruritus
>0 points but <4 points	Mild pruritus
≥4 points but <7 points	Moderate pruritus
≥7 points but <9 points	Severe pruritus
≥9 points	Very severe pruritus

ANNEXURE III - PHOTOGRAPHS



Photograph 1a: Shows the upper keloid receiving TAC injection and the lower keloid receiving intralesional Verapamil at baseline.

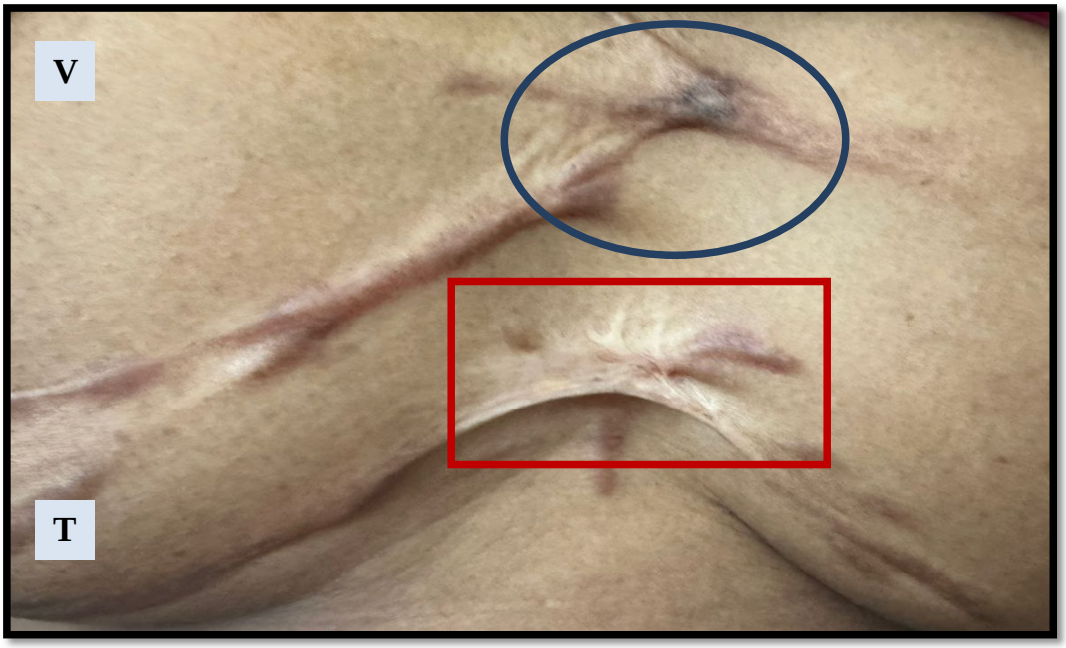
Photograph 1b: Shows the keloids at 9 weeks after intralesional therapy for 3 sessions at 3 weeks interval, showing reduction in the volume, height and visual analogue scale in both the groups.



Photograph 2a: Shows the upper keloid receiving TAC injection and the lower keloid receiving intralesional Verapamil at baseline.

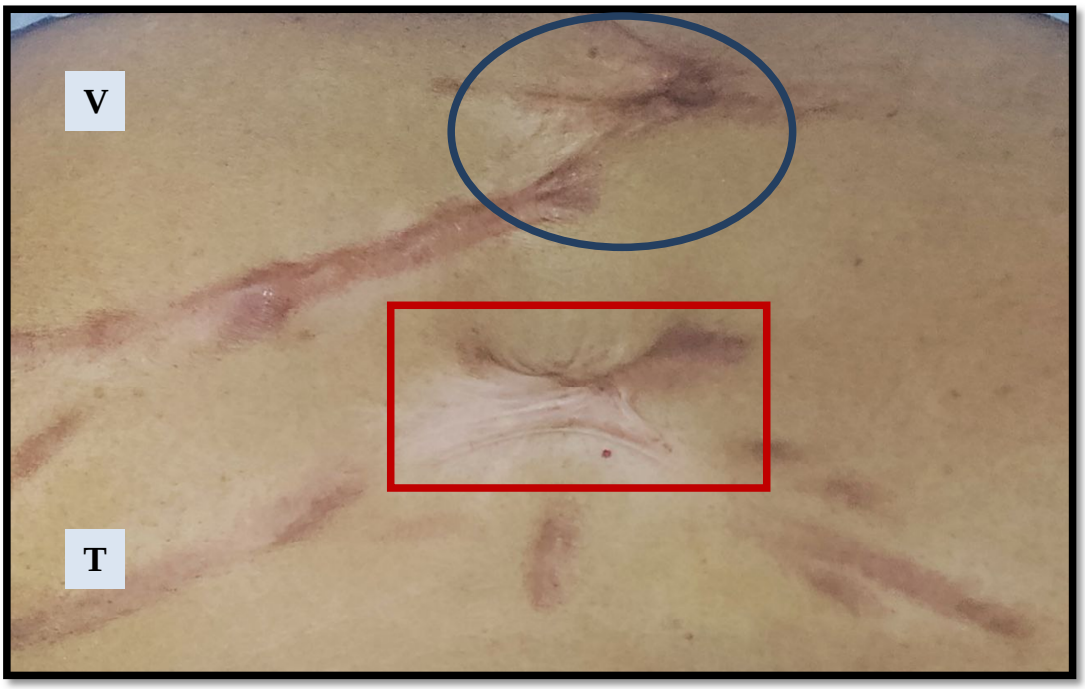
Photograph 2b: Shows the keloids at 9 weeks after intralesional therapy for 3 sessions at 3 weeks interval, showing reduction in the volume, pigmentation, height and visual analogue scale in both the groups.

O WEEKS

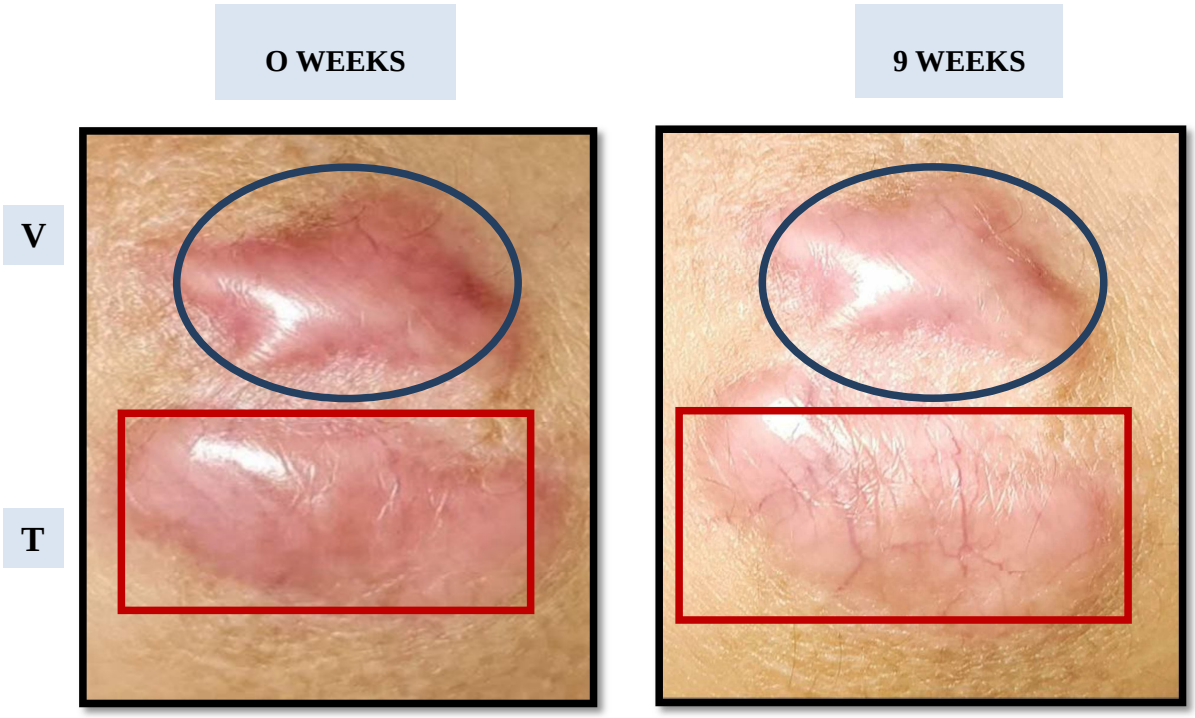


Photograph 3a: Shows the upper keloid receiving Verapamil injection and the lower keloid receiving intralesional TAC at baseline.

9 WEEKS

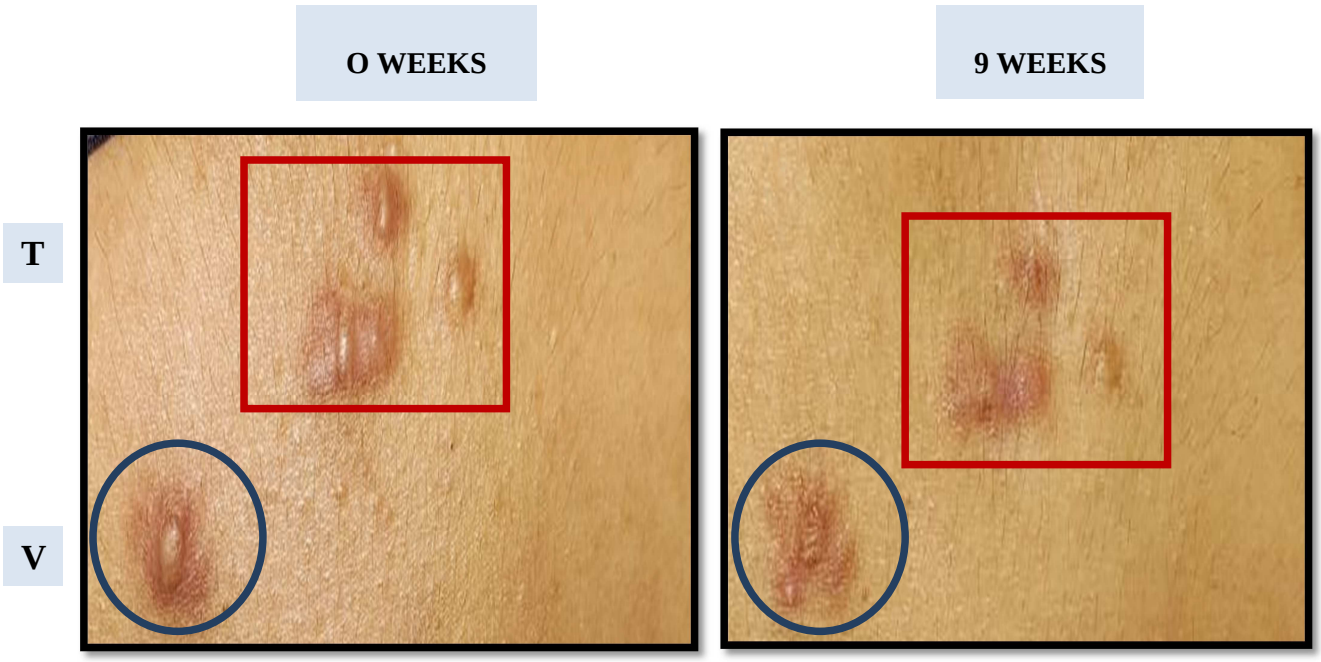


Photograph 3b: Shows the keloids at 9 weeks after intralesional therapy for 3 sessions at 3 weeks interval, showing reduction in the volume, pigmentation, vascularity, height and visual analogue scale in both the groups. TAC group had complications of hypopigmentation and atrophy at the end of 9 weeks but no such side effects were observed in the Verapamil group.



Photograph 4a: Shows the upper keloid receiving Verapamil injection and the lower keloid receiving intralesional TAC at baseline.

Photograph 4b: Shows the keloids at 9 weeks after intralesional therapy for 3 sessions at 3 weeks interval, showing reduction in the volume, pigmentation, vascularity, height and visual analogue scale in both the groups. TAC group had complication of telangiectasia at the end of 9 weeks but no such side effects were observed in the Verapamil group.



Photograph 5a: Shows the upper keloid receiving TAC injection and the lower keloid receiving intralesional verapamil at baseline.

Photograph 5b: Shows the keloids at 9 weeks after intralesional therapy for 3 sessions at 3 weeks interval, showing reduction in the volume, pigmentation, vascularity, height and visual analogue scale in both the groups. TAC group had complication of telangiectasia at the end of 9 weeks but no such side effects were observed in the Verapamil group.

ANNEXURE IV - KEY TO MASTER CHART

T	**- Triamcinolone group**
V	**- Verapamil group**
VSS	**- Vancouver scar scale**
VAS	**- Visual analogue scale**
L	**- Location of keloids**
E	**- Aetiology of keloids**
Pain score	**- Numeric pain rating scale**
Pruritis score	**- VAS pruritis score**
Pain score while injecting	**- Numeric pain rating scale while injecting**

ANNEXURE V –
MASTER CHART

Sr no.	Patient		Keloid group	Vascularity		Pigmentation		Pliability		Height		Volume (cm cube)		VISUAL ANALOGUE SCALE	
	IP NUMBER	AGE/SEX		0 WEEKS	9 WEEKS	0 WEEKS	9 WEEKS	0 WEEKS	9 WEEKS	0 WEEKS	9 WEEKS	0 WEEKS	9 WEEKS	0 weeks	9 WEEKS
1	6995093	63/M	T	3	2	2	1	3	2	3mm	2mm	1.28	0.82	1	3
			V	3	2	2	1	3	2	8mm	8mm	21.6	20.4	1	2
2	6206918	21/M	T	3	2	2	2	2	1	2mm	1mm	0.192	0.06	1	3
			V	3	0	2	1	2	1	2mm	1mm	0.12	0.028	1	3
3	6828844	19/M	T	2	0	2	2	2	0	1mm	0mm	0.02	0	1	3
			V	2	0	2	1	2	0	2mm	0mm	0.24	0.21	1	3
4	6974631	47/M	T	1	0	2	2	1	1	3mm	0mm	0.117	0	1	3
			V	1	0	2	2	1	1	2mm	1mm	0.25	0.12	1	1
5	3206760	50/F	T	3	2	2	1	5	2	3mm	1mm	3.2	0.74	1	3
			V	2	2	2	1	5	5	2mm	1mm	0.74	0.35	1	2
6	3019705	18/M	T	2	1	2	1	3	1	1mm	0mm	0.07	0	1	2
			V	1	1	0	0	3	2	2mm	1mm	0.09	0.045	1	1
7	6012536	27/M	T	3	1	2	1	4	1	3mm	2mm	0.21	0.13	1	3
			V	3	1	2	1	4	1	2mm	2mm	6.4	5.92	1	2
8	600948	52/M	T	1	1	1	1	4	4	2mm	1mm	1.2	0.42	1	2
			V	1	1	2	1	4	4	2mm	2mm	2.34	2.16	1	2
9	6515731	21/F	T	2	1	2	1	2	0	1mm	0mm	0.06	0	1	4
			V	2	1	2	2	2	1	1mm	1mm	0.069	0.044	1	3
10	7093373	27/F	T	2	1	2	1	3	1	3mm	2mm	5.28	3.2	1	4

			V	2	1	2	1	3	1	3mm	2mm	0.99	0.88	1	3
11	7089566	24/M	T	1	1	2	1	3	2	2mm	2mm	1.4	1.296	1	3
			V	1	1	2	1	3	2	2mm	1mm	1.25	0.506	1	3
12	6858955	18/F	T	3	1	2	1	3	0	1mm	0mm	0.4	0.22	1	4
			V	3	2	2	1	3	1	1mm	1mm	0.4	0.4	1	3
13	6490246	32/F	T	2	1	2	2	2	0	1mm	0mm	0.09	0.64	1	3
			V	2	2	2	2	2	1	2mm	2mm	0.3	0.24	1	3
14	7179128	65/F	T	3	3	2	1	3	2	1mm	1mm	0.25	0.2	1	4
			V	3	3	2	1	3	2	1mm	1mm	0.45	0.42	1	2
15	6123457	18/M	T	3	2	2	1	3	1	3mm	2mm	1.35	0.702	1	4
			V	3	2	2	1	3	2	3mm	2mm	1.35	0.728	1	3
16	4085980	61/M	T	3	1	2	1	2	0	2mm	0mm	0.102	0.45	1	3
			V	3	2	2	1	2	1	2mm	1mm	0.42	0.18	1	2
17	6964342	50/M	T	3	2	2	2	2	1	2mm	1 mm	3.76	2.7	1	3
			V	3	2	2	2	2	1	2mm	2 mm	0.448	0.36	1	2
18	7023381	66/F	T	3	1	2	1	3	2	2mm	1 mm	1.2	0.3	1	4
			V	3	1	2	1	3	2	2mm	1 mm	1.44	0.56	1	4
19	6111239	67/F	T	2	1	3	1	2	1	1mm	0mm	0.168	0	1	3
			V	2	1	3	2	2	1	3mm	2mm	0.231	0.09	1	3
20	6781290	35/M	T	2	1	3	2	3	2	2mm	1 mm	0.14	0.025	1	3
			V	2	1	3	2	3	3	3mm	2mm	0.135	0.06	1	2
21	7170247	35/M	T	2	1	2	1	2	1	3mm	1mm	0.3	0.03	1	2
			V	2	1	2	1	2	1	3mm	2mm	0.45	0.25	1	2
22	7161615	18/M	T	2	1	2	1	2	1	2mm	1mm	0.132	0.025	1	3
			V	2	1	2	1	2	1	2mm	1mm	0.12	0.04	1	3
23	6396642	65/M	T	3	1	3	2	3	2	2mm	1mm	1.2	0.2	1	4

			V	3	1	3	2	3	2	2mm	1mm	1.84	0.7	1	4
24	2925783	26/M	T	3	1	3	2	3	2	3mm	2mm	0.21	0.05	1	3
			V	3	1	3	2	3	2	2mm	1mm	0.09	0.03	1	2
25	6883909	21/M	T	2	1	2	1	2	1	3mm	2mm	5.64	2.7	1	3
			V	2	1	2	1	2	1	2mm	2mm	0.448	0.36	1	3
26	5729274	53/M	T	3	2	2	1	3	1	3mm	2mm	1.716	0.8	1	4
			V	3	2	2	1	3	1	5mm	4mm	2.61	1.5	1	4
27	6930414	24/M	T	2	1	2	1	2	1	3mm	2mm	0.231	0.06	1	4
			V	2	1	2	1	2	1	3mm	3mm	0.231	0.108	1	4
28	7099350	20/F	T	3	1	3	1	3	1	2mm	1mm	0.44	0.084	1	4
			V	3	1	3	1	2	1	1mm	1mm	0.088	0.07	1	2
29	7288259	19/M	T	2	1	2	2	2	2	2mm	1 mm	1.44	0.45	1	4
			V	2	1	2	2	2	2	2 mm	1 mm	0.64	0.216	1	4
30	7145765	55/M	T	3	2	2	1	3	2	3mm	1mm	1.8	0.2	1	4
			V	3	2	2	1	3	2	3mm	1mm	2.76	0.7	1	3
31	6324516	62/M	T	3	1	3	2	3	1	2mm	1mm	0.5	0.06	1	4
			V	3	2	3	2	3	1	2mm	1mm	0.154	0.056	1	3
32	452637	23/M	T	3	1	3	2	3	1	3mm	1mm	1.8	0.2	1	4
			V	3	1	3	2	3	1	3mm	2mm	2.76	1.4	1	3
33	876537	27/M	T	2	1	2	1	2	2	2mm	1mm	0.44	0.042	1	3
			V	2	2	2	2	2	2	2mm	1mm	0.176	0.063	1	3