"A COMPARATIVE STUDY OF EFFECTIVENESS OF CRYOTHERAPY WITH INTRALESIONAL TRIAMCINOLONE VS FRACTIONAL CO2 LASER WITH TOPICAL BETAMETHASONE FOR THE TREATMENT OF KELOIDS"

By

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Dissertation submitted to the

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In partial fulfillment of the requirements for the degree of

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IN

DERMATOLOGY, VENEREOLOGY AND LEPROSY

Under the guidance of

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APRIL/MAY 2022

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LIST OF ABBREVIATIONS

ACE	Angiotensin converting enzyme
ATP	Adenosine triphosphate
BTX-A	Botulinum toxin type A
CO_2	Carbon dioxide
ECM	Extracellular matrix
FGF	Fibroblast growth factor
G	Gauge
G6PD	Glucose-6-phosphate deficiency
Gy	Gyrate
HGF	Hepatocyte growth factor
HLA	Human Leukocyte Antigen
IFN	Interferon
IGF	Insulin like growth factor
IL	Interleukin
ILS	Intralesional steroid
IPL	Intense pulsed light
IU	International unit
LCs	Langerhans cells
LED	Light Emitting diode
LN2	Liquid nitrogen
M6P	Mannose -6-phosphate
MAP	Mitogen activated protein
MMPs	Matrix metalloproteinases

MSH	Melanocyte stimulating hormone
MSS	Manchester Scar Scale
mTOR	Mammalian target of rapamycin
MTX	Methotrexate
Nd:YAG	Neodymium-doped: Yttrium Aluminium Garnet
PCNA	Proliferating cell nuclear antigen
PDGF	Platelet derived growth factor
PDL	Pulsed dye laser
POSAS	Patient observer scar assessment scale
RCT	Randomized controlled trials
SERM	Selective estrogen receptor modulator
SGS	Silicone gel sheets
TGF	Transforming growth factor
Th	T-helper cell
TLR	Toll like receptor
TNF-α	Tumor necrosis factor alpha
VAS	Visual Analogue Scale
VEGF	Vascular endothelial growth factor
VSS	Vancouver scar scale
5-FU	5-fluorouracil
VDRL	Venereal Disease Research Laboratory
α-SMA	Alpha-smooth muscle actin

ABSTRACT

INTRODUCTION

Keloids occur as a hyperproliferative response of dermal connective tissue to trauma. Their management remains a challenge for practitioners as there is still no single universally accepted treatment, leading to recurrences which are frustrating for patients and clinicians alike. Unlike monotherapy, combination therapies have proved to produce better response rates. Hence, it becomes essential to compare the upcoming combination therapies to determine a modality with highest efficacy, least recurrence and produces good aesthetic results.

OBJECTIVES

1) To compare the therapeutic effectiveness of cryotherapy with Intralesional Corticosteroid and Fractional CO2 laser followed by Topical Corticosteroids in the treatment of keloids.
2) To assess the efficacy of Fractional CO2 laser with Topical Steroid in the treatment of keloids.
3) To assess the efficacy of Cryotherapy with Intralesional Corticosteroid in the treatment of keloids.

MATERIALS AND METHODS

A comparative study conducted in Department of Dermatology, Venereology and Leprosy in R.L.J Hospital and Research Centre attached to Sri Devaraj Urs Medical College from December 2019 and May 2021. 170 patients were randomly allocated in two different regimens of 85 each to receive a combination of cryotherapy with intralesional triamcinolone

acetonide (40mg/ml) injection and laser ablation of keloid followed by topical corticosteroid application, twice a day, until the next treatment session. Patients were given 4 treatment sessions each and were evaluated after each treatment session to look for improvement.

For quantitative variables, mean and standard deviation were used, whereas for categorical variables, frequency and proportion were used. Appropriate tests were used to perform inferential statistics. Statistical significance was defined as a P value of less than 0.05.

RESULTS

There was remarkable difference in the treatment outcome of both the group, with group 2 showing more improvement (p value < 0.001) and markedly fewer side effects (p value < 0.001) like atrophy, pigmentation abnormality, etc. as compared to group 2 patients. Patients in group 2 had less pain as compared to patients in group 1, making them more compliant to treatment. Majority (31.8%) of patients belonged to 31-40 years of age group. The most common reason for treatment was for cosmetic concerns, seen in 70.6% of the patients.

CONCLUSION

Both combination regimens showed excellent responses with minimum recurrence rates, indicating high efficacy in management of keloids. Regimen I, however, was associated with more troublesome and persistent adverse effects signifying regimen II to be safer for the treatment of these exuberant scars.

KEY WORDS: Keloid, combination therapy, cryotherapy, triamcinolone acetonide, Laser-assisted drug delivery, topical steroids

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INTRODUCTION

INTRODUCTION

Keloids occur as a hyperproliferative response of dermal connective tissue to trauma. Wound healing is a complex biological process that involves various cell-to-cell and cell-to-matrix interactions in a complex environment of local and systemic stimuli. Overhealed wounds, such as keloids, form when this healing process goes awry.

Keloids are irregular, hypertrophic lesions which most commonly occur in areas of high skin tension such as the chest region and extend beyond the original borders of the wound or inflammatory response. They may follow local skin trauma or inflammatory skin disorders like lacerations, tattoos, burns, injections, ear-piercing, vaccination, bites, acne, abscess or surgery. They are also known to occur spontaneously.

Besides posing as a cosmetic concern, causing social discomfort, psychological stress and embarrassment, these unsightly exuberant scars may also cause remarkable pain, pruritus, hyperesthesia and possibly affect joint movement. They seldom regress over time and have a major negative impact on one's quality of life.

Keloids continue to be a problem for both patients and doctors. There is no universally approved treatment that results in permanent keloid scar ablation, despite the fact that different therapeutic procedures with treatment guidelines and recommendations have been published throughout the years. Monotherapy especially shows variable and transient results. Combination therapies, however, have proved to produce better response rates with reduced incidence of recurrences.

This study has been undertaken to assess and compare the efficacy of two such combination therapies, namely the intralesional injection of triamcinolone with cryotherapy versus combination of Fractional CO2 with topical betamethasone, in achieving good cosmetic response.

This research looked at age, sex, location, predisposing variables, and family history in addition to the treatment features.

AIMS & OBJECTIVES

OBJECTIVES

OBJECTIVES OF THE STUDY

1) To compare the therapeutic effectiveness of cryotherapy with intralesional corticosteroid and fractional CO2 laser followed by topical corticosteroids in the treatment of keloids.
2) To assess the efficacy of fractional CO2 laser with topical steroid in the treatment of keloids.
3) To assess the efficacy of cryotherapy with intralesional corticosteroid in the treatment of keloids.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HISTORICAL ASPECTS

Smith Papyrus was the first to describe keloids in 1700BC, as "the existence of swelling on the breast, large, spreading, hard, touching them is like touching a ball of wrappings." [1,2]

The **Olmec tribes**, who lived in the region that is now Mexico, used keloids and hypertrophic scars as body decoration from 1500 to 1000 BC.[3]

Retz described keloids, under the name **"Dartre de graisse",** as a cicatricial tumor of the skin, which he thought was of spontaneous origin.[4]

Baron Jean-Louis Albert, a French dermatologist, in 1806, identified and defined keloid as an entity, initially calling it "cancroide" and later changing it in 1816 to "cheloide", derived from the Greek "chele", meaning crab's claw.[3,5,6]

Yorubas have been known to record the presence of keloids ten centuries before Retz and Alibert. They recognized, for example, that keloids often appear in certain families, but does affect all members. They also knew about the time interval between infliction of trauma and development of the lesion. Indigenous customs of facial markings and carbolic perforation were frequently performed around 7th day of birth. However, a delay in the scarification process could lead to keloidal formation if done in adolescence or adult life, according to Yoruba. The Yorubas also seemed to know that once a lesion developed, it grew in size and had no remedy, except when "the divine Power is suitably appropriated to intervene in bringing about its resolution".[7-9]

Hawkins described lesions that could be keloids in 1835 and **Macphearson** added to the early works on keloids.[10,11]

Addison in 1854, introduced the term "true keloid" (arising spontaneously) and categorized lesions described by Albert as "false keloids" (ones which arise at sites of trauma). Later it turned out that the lesions he described were possibly either scleroderma or morphea and hence his nomenclature of true/false keloids was discarded.[12,13]

McCoy and Cohen in 1981 described keloids as clinically vexatious scars characterized by excessive collagen accumulation.[14]

Although, keloids were primarily thought to develop only in humans but comparable lesions have been reported in other animals, e.g.- horses, cattle, dogs and on the feet of vultures and eagles. However, they are not good prototypes to study wound repair as the excessive collagen that gets deposited is reabsorbed in animals, when the tissue insult ceases.[15,16]

GENERAL CONSIDERATIONS

Definition:

Keloids are benign, dermal, fibro proliferative tumors, characterized by increased collagen formation at the site of previous skin injury in a predisposed individual. They extend beyond the borders of actual wound, invade the surrounding skin and do not regress spontaneously.[17]

Nomenclature:

Jean Louis Albert (1768-1837), in 1816, proposed the word "cheloide", Greek derivative of "chele" meaning "crab's claw" and "oide" meaning "like". He had originally called it "cancroide" in 1806, but it was later changed to avoid misunderstanding of it being cancer and its association.

He wrote a chapter titled “Les carcroidesou keloids”, and in his text used the term for first time, which was later accepted by the English, the Americans and German dermatologists.[5,6,18]

CLASSIFICATIONS

“Arnold in 1959 proposed two important classifications of keloids.[19]

I. CLINICO-MORPHOLOGICAL CLASSIFICATION

a. Acute

b. Subacute

c. Chronic

II. ETIOLOGICAL CLASSIFICATION

1. Due to injury

a. Mechanical

b. Burns

c. Electrocautery

2. Due to inflammation

a. Acne

b. Varicella

c. Vaccination especially intradermal

d. Furuncles, etc.

3. Miscellaneous

a. Incisions

b. Following surgeries such as thyroidectomy, thoracotomy, nephrectomy.

c. Skin grafting, etc."

ETIOLOGY

The understanding about the exact etiology and nature of keloids is limited.

Trauma:

In majority of patients, trauma has been proposed as the main triggering factor. This trauma can range from a simple scratch, insect bite, abrasion, post-vaccination, acne, chicken pox, surgical procedures or burns (chemical or thermal). Due to the development of spontaneous keloids on non-traumatized areas and lack of development of these lesions following cutaneous trauma, especially over the leg, has led to the belief in the presence other predisposing factors other than trauma in the formation of keloids.[5]

Keloids have been observed more commonly on areas with increased skin tension. Incision across Langer's lines with a subsequent increase in skin tension has also been suggested.[20-23] Increased skin tension due to firmly braided hair is seen in several parts of Africa and is becoming increasing popular in the United States, leading to the formation of "Coiffure keloids" on the scalp.

Asboe-Hansen discovered that long standing dermal oedema causes increased levels of muco-polysaccharide content in the skin, thereby stimulating the deposition of collagen fibers and consequently leads to keloid formation.[24,25]

According to "Sebum Autoimmune Hypothesis" of keloid formation proposed by Osman and associates, cutaneous trauma may cause intradermal secretion of sebum from the functioning sebaceous glands. This sebum acts as an antigen, commencing an autoimmune granulomatous response that might end with "keloid" formation. The absence of keloids over the palms, soles, lips and areas lacking sebaceous glands further supports their theory.[26]

Few investigators suggested the presence of foreign body and not any type of trauma may incite a keloid formation. Johnson in 1969 cited the presence of suture debris and grime in wound as probable provocative factors.[27-30]

Infection:

Infections, either bacterial or viral, has found to be a contributory factor in the development of keloids. It is the trauma caused by these infections rather than the infectious agents that possibly incites the lesion formation.[31]

Although tubercle bacilli was thought to cause keloids, a study with 168 keloid patients did not report even a single patient with clinical evidence of tuberculosis and positive tuberculin reaction patients were in the range of what would be seen in the standard population. Keloids may follow varicella, small pox, herpes zoster or furuncles. Although few cases have reported that syphilis may promote the development of keloids, a study with 200 keloid cases found only one patient having syphilis.[32-35]

Hormonal Factor:

Although keloids have been related with several endocrinological factors, there is no certainty of the same. Hormones secreted by the thymus gland, thyroid and parathyroid glands, ovary and pituitary, either alone or in combination have been incriminated.[32]

FACTORS AFFECTING KELOIDS

Age: Keloids can develop at any age, but they are most frequent during and after puberty. Keloids were determined to be less than 30 years old in 88 percent of patients. They are found to be uncommon in the very young due to low trauma frequency and severity. Keloids are also found to be uncommon in the very old and keloidal regression has been reported after menopause.[7,8,12,13,31]

The explanation of these findings include[36]:-

1) Young people are more frequently subjected to trauma.
2) Young skin is tauter compared to the redundant skin in the elderly.
3) The rate of collagen synthesis also occurs at a higher rate in younger patients.

Sex: Keloids have been found to be more common in female patients than in male patients. This could be attributed to the fact that girls are more concerned about their appearance and have a higher rate of earlobe piercing than males.[15]

Race: There is a higher incidence of keloids in darkly pigmented individuals of African, Hispanic and Asian ancestry when compared with Caucasians. From 4.5% to 16% of predominantly black and Hispanic populations have keloids with an incidence being as high

as 16% in Africans.[36] Polynesians and Chinese are reported to be affected more often in than Indians and Malaysians. Caucasians and albinos are affected the least.

The hypothesis for this finding presented by Koonan states[37]:

1. Keloids are more common in dark-skinned people, whose melanocytes are more responsive to melanocyte stimulating hormone (MSH).
2. Keloid development is more common in dark-skinned people of all ethnicities than in fair-skinned people.
3. Keloids are more common in areas with a high concentration of melanocytes. That is why keloids are uncommon on the palms and soles, where the number of melanocytes is low.
4. Keloids are more common during puberty and pregnancy, both of which are states of physiological hyperactivity, with pituitary stimulation being linked to enhanced pigmentation.

Site: Keloids are particularly common in areas with high skin tension, such as the chest, deltoid region, upper back, and back of the neck. They're also visible in low-tension places like the earlobes. Keloids have been documented on the genitalia (after circumcision or trauma), cornea (after corneal damage), palms, and soles on a rare basis. Keloids are typically found in locations where the skin is thick.[38]

"Crockett has proposed three orders of susceptibility[37]:

1. **First order-** In susceptible individuals, all scars in certain areas are likely to develop into keloids, namely in the presternal area, upper back and deltoid region.
2. **Second order-** The nature of injury can impact the ability to form keloids in areas such as the beard region, the upper extremity, the anterior chest (including the midline), the scalp and the forehead.

3. **Third order-** In certain areas, keloid formation is quite unusual and almost never seen, such as the lower back, abdomen, lower limb, central face, eyelids and genitalia. The significance of these locational differences remains unexplained."

Hormones: Hormones generated by the pituitary glands, thyroid and parathyroid glands, thymus gland, and ovaries have been linked to the development of keloids, either alone or in combination.[32]

Keloids are more common in acromegalics, pregnant women, and adolescents, all of whom experience physiological pituitary hyperactivity. Growth hormone, which accelerates the creation and deposition of collagen fibrils, could be to blame for this phenomenon.[24,39,40]

Keloids are also observed to be more common in areas of hyperpigmentation, which could be linked to hyperthyroidism, pregnancy, or puberty. It's been suggested that in these circumstances, MSH is secreted in excess, and the melanocytes are more sensitive to it.[27]

Genetics: Transmission has been reported as both autosomal dominant and autosomal recessive. Patients with HLA–B14, HLA-B21, HLA-BW16, HLA-BW35, HLA-DR5, HLA-D1W35, HLA-DRB1 and HLA-DQB1 are associated with an increased risk of keloidal scarring. Dr. Jones and colleagues, on using advanced genetic sequencing technology to profile the genomes of six keloids and six normal skin samples, revealed 152 keloid specific genes, of which 10 genes were involved in biological pathways known to be important to the process of keloid development.[1,3]

Blood Group: Keloids are commonly seen in patients with blood group A.[1]

PATHOPHYSIOLOGY

As the exact pathophysiology of keloid is not fully understood, various hypotheses have been postulated.

1. Altered Growth Factor Milieu

Increased growth factor activity (transforming growth factor and platelet derived growth factors) and alterations in the extracellular matrix (fibronectin. hyaluronic acid and biglycan) have contributed to the exuberant scar formation in keloids.[41]

A. Growth Factor Differences

Transforming growth factor sensitivity is increased in keloid fibroblasts (TGF). TGF levels have been found to be significantly higher in areas of increased proliferation and collagen deposition inside keloid tissue in studies. Similar to TGF, keloids have a four to five fold increase in platelet derived growth factor (PDGF) receptors, and their growth stimulatory effects are synergistic.[41]

B. Extracellular Matrix Differences

Keloids have an unusual extracellular matrix (ECM), with higher quantities of fibronectin and proteoglycans and lower levels of hyaluronic acid. The fibrotic character of keloids is caused by their defective regulation. Collagen architecture is influenced by proteoglycans such as biglycan and decorin, which bind to collagen fibrils. As a result of their abnormal production, the extracellular matrix and collagen architecture becomes chaotic.[42-44]

Three concepts address the unusual growth factor milieu in keloids:

Concept 1- Interactions between epithelial and mesenchymal cells may play a key role in keloid development. Keloid keratinocytes create a keloid phenotype in normal fibroblasts,

according to studies using in-vitro keratinocyte-fibroblast co-culture systems. Dermal fibroblastic activity is linked to histopathological alterations in the keloid epidermis.[45]

Concept 2- In fetal cells, the proliferative pathways are active but in adult life they are inactive. This pathway becomes active again in keloids. Fetal and keloid tissues can survive and proliferate in a reduced serum environment in vitro, unlike the normal adult skin fibroblasts.[46]

Concept 3- Hypoxia in keloids may cause the release of angiogenic growth factors, which promote endothelial proliferation, delay wound maturation, and increase fibroblast collagen production. Micro vessels in scars are occluded due to abundant endothelial tissue, resulting in hypoxia in keloids, according to transmission electron microscopy.[47,48]

2. **Collagen Turnover Hypothesis**

Keloids have a particular physical appearance because of disruption in collagen equilibrium. Collagen bundles in keloids are more numerous, thicker, and wavier, and they are grouped in an unorganized way, as seen under optical and electron microscopy. At the ultrastructural level, the signature "collagen nodules" can be seen. When keloids are compared to normal skin or scars, the proportion of type I to type III collagen is much higher, and this difference is due to control at both the pre-transcriptional and post-transcriptional stages.[49-52]

3. **Tension Hypothesis**

Fibroblast proliferation and collagen synthesis are stimulated by mechanical strain. Stretch and tension have been shown in vitro and in vivo investigations to not only drive collagen formation, but also to influence collagen architecture and orientation, as well as dermal remodeling. Incisions perpendicular to muscle fibers should ideally heal with collagen

oriented naturally since collagen is oriented perpendicular to muscle contractions. As a result, incisions along to skin tension lines seldom result in aberrant scars, whereas incisions near joint motion locations commonly do. Keloid development can also be reduced by using absorbable subcuticular sutures instead of non-absorbable interrupted sutures. It is also observed that abnormal scarring rarely occurs in the elderly, whose skin has characteristically poor tension.[53,54]

4. Genetic Immune Dysfunction

Due to its association with particular HLA subtypes, keloids may be formed as a result of an inherited abnormal immune response to dermal injury. Familial tendencies indicate a polygenic inheritance patterns. Over 152 keloid specific genes, of which 10 genes were a part of biological pathways known to be important to the process of keloid development have been identified. In patients with keloids, higher levels of serum immunoglobulin E have been linked to an increased risk of allergic diathesis. Multiple studies have discovered comparable patterns in serum complement, immunoglobulin G, and immunoglobulin M levels in keloids patients, implying a systemic immunological state that is genetically prone to keloid formation.[55]

The production of keloidal scars is now recognized as an autoimmune connective condition. Antifibroblast antibodies circulating in the blood attach to fibroblasts and induce collagen formation and proliferation, similar to antithyroid antibodies in Hashimoto's thyroiditis. Keloids have been linked to inherited connective tissue disorders such as "Rubinstein-Taybi syndrome, Ehlers-Danlos syndrome, progeria, osteopoikilosis, scleroderma, and pachydermoperiostosis," according to research. Clinical research also suggests that people with keloids have a cell-mediated immune system that is innately hypersensitive.[55]

Keloids with a delayed initial growth and a quick secondary growth show the presence of a local immunological reaction. When monofilament suture material is used to close surgical incisions instead of multifilament suture material, there are fewer aberrant scars, possibly due to reduced local inflammation.[56]

Studies also showed that "actively growing keloid explants, placed into nude mice that lack an immune system, grow initially and then regress despite revascularization. This regression supports the theory that systemic immune response directed the growth of keloids before their explantation".[55-57]

5. Sebum Reaction Hypothesis

Keloids, according to this theory, are the result of an immunological response to sebum, which acts as an antigen and is released intradermally after trauma. Mast cell chemotaxis and fibroblast collagen production are stimulated by the release of cytokines, particularly interleukins and TGF-. Pilosebaceous units on the advancing border are disrupted as the keloid spreads, and the process continues.

The presence of keloids on areas with a high concentration of sebaceous glands, such as the chest wall, shoulder, and pubic area, supports this notion. They're rare on the palms and soles, which don't have any sebaceous glands.

This idea also explains why two apparently identical lesions form one keloid and one regular scar in the same person.

This theory also explains why keloid scarring affects exclusively humans, the only mammals with real sebaceous glands.

In patients with keloidal tendencies, a favorable skin reaction to intradermal sebum antigen can be evoked, with a larger consequent wheal size. Keloids can also occur after autologous skin immunization, and a sebum vaccine can successfully desensitize individuals from keloid recurrences after excision.[58]

Radiation therapy and steroids are effective in treating keloids because the former reduces sebum production while the latter suppresses local lymphocytic activity, implying that sebum reaction is the source of keloid formation. It is thought that ablation of the pilosebaceous unit prior to elective surgical excision may avoid the production of keloids later.[58-60]

PATHOGENESIS

The typical sequence of wound healing must be grasped in order to comprehend the pathophysiology of keloids.

Normal wound healing occurs in three phases:

1. The inflammatory phase

2. The proliferative or granulation phase

3. The maturation or remodeling phase

The "**first inflammatory phase**" occurs when the coagulation cascade is activated, causing the release of cytokines that stimulate the chemotaxis of non-specific immune cells (such as macrophages and neutrophils) into the wound for early wound debridement.[43]

The "**proliferative phase**" which lasts three to six weeks, begins after 48 to 72 hours. Fibroblasts are drawn to the wound and begin the production of granulation tissue, which is made up of procollagen, elastin, proteoglycans, and hyaluronic acid. This serves as the framework for vascular ingrowth structural healing. Physiological wound contraction is mediated by myofibroblasts that include myofilaments (SMA, desmin).[44]

Once the lesion is closed, the young scar might enter "**the maturation period**" which can last several months.[43,44,61]

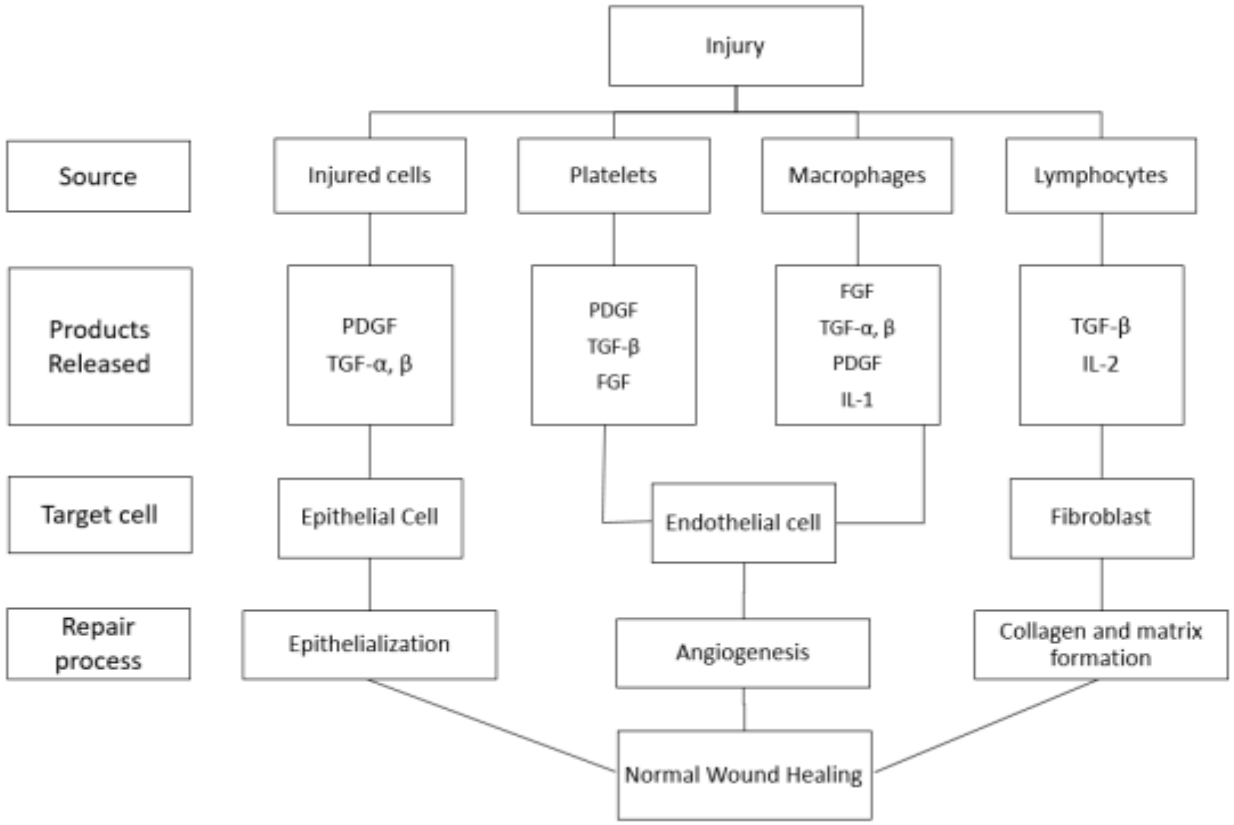


FIGURE A: NORMAL WOUND HEALING

Type I and III collagen are the most common, with types IV and V appearing in minor amounts. Type I collagen makes up the majority of skin collagen, with type III accounting for only 20% of adult skin collagen.

Keloids produce 20 times more collagen than normal, unscarred skin, with a higher type I to type III collagen ratio. To downregulate type I collagen in keloids, neither pre-transcriptional nor post-transcriptional pathways are effective.[44]

Various signaling molecules govern wound healing at the molecular level, including growth factors [TGF-β, PDGF, and VEGF], mitogen-activated protein (MAP) kinases, matrix metalloproteinases (MMPs), and tissue inhibitors of metalloproteinases.[44]

Keloid development is caused by any disruption in the complex wound healing process.

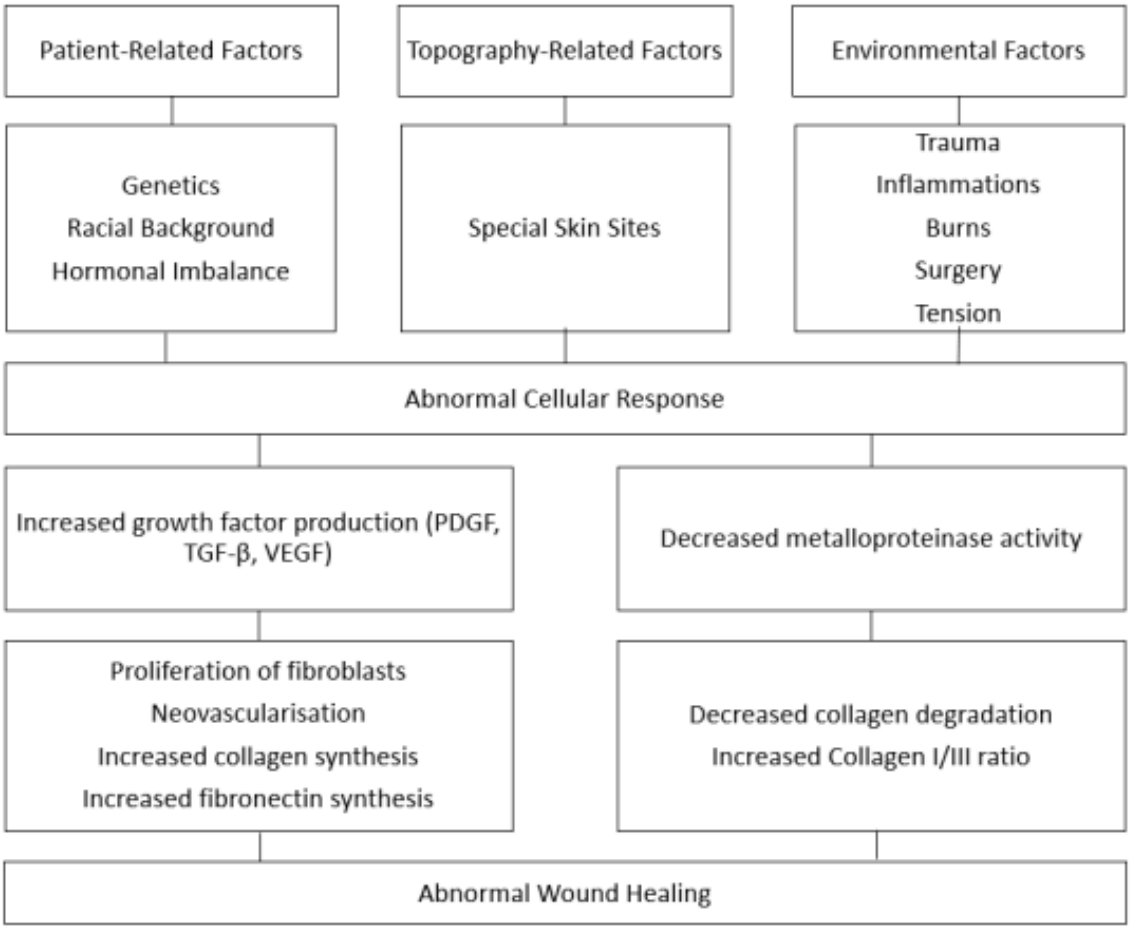


FIGURE B: PATHOGENESIS OF ABNORMAL WOUND HEALING

Molecular and Cellular Pathology

1- Epidermal-Mesenchymal Interaction

Langerhans cells (LCs) and keratinocytes are epidermal cells that signal the dermis to cause granulation tissue and scar formation, as well as remodel the ECM. Keloid formation may be aided by an increase in the number of LCs, as well as lower levels of IL-1α (Interleukin 1α) and higher levels of IL-4.

Keratinocyte-derived growth factors including IL-1α, IL-1β, TNF (Tumor Necrosis Factor-α), PDGF, TGF-β, and fibroblast growth factor (FGF) are involved in the production of

granulation tissue and dermal matrix remodeling. Th-2 cells can increase collagen formation, whereas Th-1 cell release of interferon-gamma (IFN-γ) can prevent their release, making keloid an inflammatory dermatosis.[62, 63]

TGF-β controls cell proliferation and differentiation, embryonic development, wound healing, and angiogenesis in its inactive state. TGF-β is generally shut off after wound repair is complete. It is overproduced and poorly controlled in keloids due to normal autocrine signaling processes.

Furthermore, keloid fibroblasts have a higher number of growth factor receptors and hence respond more strongly to growth factors like TGF-β and PDGF. Reduced MMP synthesis could possibly be to blame for the lack of scar regression in keloids.[64]

2- Cutaneous tissue Angiotensin–Converting Enzyme (ACE) activity

In keloids, ACE activities are higher than in normal or damaged skin. As a result, angiotensin-converting enzyme inhibitors and angiotensin-1 receptor blockers may be useful as innovative therapeutic agents in the treatment of persistent keloids.[65]

3- Metabolic Activity

Keloids contain higher Adenosine Triphosphate (ATP) levels and fibroblasts than pink or white scars.

Nitric oxide, a free radical, stimulates fibroblast collagen synthesis and is present in higher concentrations in keloids.

Factor XIIIa has transglutaminase activity, which produces fibrin crosslinking during the last stages of blood coagulation and induces fibroblast growth. They're also seen in keloids in substantially higher concentrations than in normal skin.[65]

4- Apoptosis

After a tissue damage, apoptosis, or programmed cell death, plays a role in the transition from granulation tissue to scar formation.

The p53 tumor suppressor gene has been connected to apoptotic pathways through its effect on bcl-2 gene expression. In the younger, high-cell density sections of keloid, focal deregulation of p53 paired with overexpression of bcl-2 may result in a combination of enhanced cell proliferation and decreased cell death.[66]

Insulin-like growth factors (IGF) I and II, mitogen and other inhibitors of apoptosis protect the keloid from apoptosis.[65,66]

HISTOPATHOLOGY

The histological features of keloids and hypertrophic scars appear to be similar under light microscopy, however scanning electron microscopy reveals major morphological distinctions between normal human skin, keloids, and hypertrophic scars.

Collagen bundles can be detected in normal skin, the majority of which run parallel to the epithelial skin. Fibrillar collagen strands appear to be haphazardly connecting these bundles to other collagen bundles.[67]

Collagen bundles in hypertrophic scars are flatter, less defined, and appear to be grouped in a wavy pattern. The majority of the bundles, on the other hand, appear to be parallel to the epithelium surface. At the periphery, they often have a capsule-like band. At the periphery, blood vessels can be found. Although both keloids and hypertrophic scars have enhanced gene transcription of α1(I) procollagen, hypertrophic scars' increased mRNA concentration is compensated at the post-transcriptional level, whereas keloids' is not.[68]

In keloids, beneath a normal epidermal layer, collagen bundles are virtually non-existent and the fibers lie in haphazardly connected, loose sheets that appear randomly oriented to the epithelial surface. The collagen fibers are larger, thicker, more eosinophilic and wavier than those in hypertrophic scars. Keloids also show increased fibroblast proliferation rates.[67,68]

Enzyme concentrations such as alanine transaminase and metabolic activities marked by adenosine triphosphate are also elevated in keloids. Proteoglycans are also present in excess amounts in keloid scars. There is decreased concentration of adnexal structures.[69-73]

There are four histological features that are considered pathognomonic for diagnosis of keloids[48]:

1. Presence of keloidal hyalinized collagen
2. A tongue like advancing edge underneath normal-appearing epidermis and papillary dermis.
3. Horizontal cellular fibrous bands in the upper reticular dermis
4. Prominent fascia like fibrous bands.

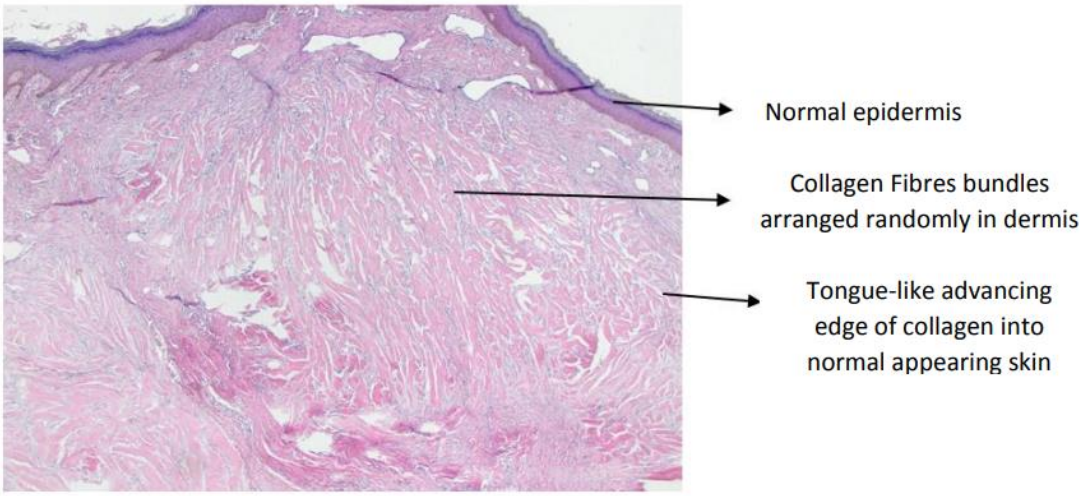


FIGURE C: HISTOPATHOLOGY OF KELOID

FEATURES	HYPERTROPHIC SCARS	KELOIDS
Collagen bundles	Fine, well organised, wavy, parallel to epidermis	Large, thick, closely packed ,random to epidermis
Myofibroblasts	Present	Absent
Alpha-SMA expressing	Nodular formation	Around blood vessels wall
PCNA expressing	Low expression	High expression
Hyaluronic acid localization	Major component, papillary dermis	Thickened, granular /spinous layer
Mucin deposition	Negative	Focal expression in dermis
ATP level	Low expression	High expression
Amorphous substance on electron microscopy	Absent	Diffuse pattern
Apoptosis	Decreased	Increased/decreased
P53 levels	Low	High

TABLE 1: BIOCHEMICAL AND MOLECULAR DIFFERENCES BETWEEN KELOIDS AND HYPERTROPHIC SCARS[48]

CLINICAL FEATURES

Keloids have different clinical symptoms depending on the underlying trauma. Keloids usually appear months after a trauma or skin damage. Few keloids appear on their own, and patients may have no recollection of the event that caused them.[74]

Site

Keloids can appear on any part of the body, but particular locations, such as the deltoid region, presternal area, upper back regions, and earlobes, are more susceptible to them.[67,75,76] Rarely, keloids have been reported over cornea, palms, soles and genitalia.[74]

Number of lesions

The majority of patients have one or two keloids, whereas a small percentage of patients, particularly those who acquire keloids spontaneously or as a result of acne or chicken pox, have many lesions.

Size

The size of the tumor might range from a little papule to a big tumor. They protrude over the surrounding skin's level, but only rarely reach the underlying subcutaneous tissue. Lesions on the ear, neck, and belly are generally pedunculated, but those on the central chest are elevated with a flat surface, with the base often wider than the top.

Shape

Most are round or oval with a regular margin, while others have a claw-like configuration with irregular borders.

Consistency

Range from soft and doughy to rubbery hard.

Color

Initially, keloids are erythematous, later turning brown and then pale as they age.

Surface

Keloids usually have a smooth surface devoid of hair follicles and other functioning adnexal glands.

Course

Keloids grow in size slowly for weeks to months after they appear (at times years). They can sometimes grow quite quickly, doubling in size in a month. Keloids become stable and asymptomatic once their growth ends. They rarely regress on their own, despite the fact that spontaneous regression has been linked to growing older. A keloid that had been present for 40 years has been documented to spontaneously retreat.[5]

Although some keloids are known to be tender, painful, pruritic, and may create a burning sensation, most patients seek medical intervention for cosmetic reasons.[74]

DIFFERENTIAL DIAGNOSIS[48]

1. Hypertrophic scars
2. Dermatofibrosarcoma protuberans
3. Trichilemmal carcinoma
4. Keloidal basal cell carcinoma
5. Apocrine cystadenoma
6. Adult-onset xanthogranuloma
7. Mixed tumour
8. Chronic folliculitis

HYPERTROPHIC SCARS	KELOIDS
Develop soon after surgery	May not begin for months following trauma
Usually regresses with time (maturation)	Rarely regresses spontaneously
Limited boundaries	Overgrow their boundaries
Size commensurate with injury	Minor injury may produce a large lesion
Occurs with motion (compression)	Independent of motion
Usually occurs over the flexor surface like joint, abdomen etc	Areas of high predilection like earlobe, presternal area and rarely across joints
Improves with appropriate surgery	Often worsened by surgery

TABLE 2: CLINICAL DIFFERENCES BETWEEN HYPERTROPHIC SCARS AND KELOIDS[74]

Keloids and hypertrophic scars may also be biochemically differentiated using magnetic Resonance Imaging (MRI), by correlating water proton relaxation time with duration of scar. (Babu et al[77])

ASSESSMENT OF KELOIDS

There is a lack of standardized methodology and systematic approach in the assessment of scars. Refinement of these assessment methods may facilitate treatment and may even prevent scar formation.

Factors to be considered include[78]:

1. Scar height or thickness
2. Pliability
3. Surface area
4. Texture
5. Pigmentation
6. Vascularity

GRADING/SCORING SYSTEMS

1. Vancouver Scar Scale (VSS)

The VSS is perhaps the most well-known burn scar assessment method, having been first reported by Sullivan in 1990. It measures vascularity, height/thickness, pliability, and pigmentation, among other things. The final score does not take into account the patient's impression of his or her scar.

This scale is useful in evaluating therapy and measuring the outcomes in scar studies.[79-81]

Variables	Scar characteristics	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
	Contracture	5
Height	Flat	0
	<2 mm	1
	2-5 mm	2
	>5 mm	3
Total		**13**

TABLE 3: THE VANCOUVER SCAR SCALE

2. Visual Analogue Scale (VAS)

The multidimensional VAS is a photograph-based scale derived from evaluating standardized digital photographs in 4 dimensions, viz. pigmentation, vascularity, acceptability and observer comfort, plus contour. The individual scores are summed up to get a single overall score ranging from “excellent” to “poor”. It has demonstrated high observer reliability and internal consistency, when compared to expert panel evaluation. However, this scale has shown only moderate reliability when used among lay panels.[82,83]

3. Patient and Observer Scar Assessment Scale (POSAS)

This scale adds to the objective data collected by the VSS by allowing for subjective evaluation of symptoms such as pain and itching. The Patient Scar Assessment Scale and the Observer Scar Assessment Scale are the two numerical scales that make up the system. Vascularity, pigmentation, thickness, relief, pliability, and surface area are all assessed. The patient's rating of pain, itching, color, stiffness, thickness, and alleviation is also included. Although it incorporates subjective pain and pruritus symptoms, it does not include a functional assessment of whether the pain or pruritus affects quality of life. When compared to the VSS, the POSAS has demonstrated internal consistency and inter-observer reliability in assessing postsurgical scars and linear scars following breast cancer surgery, with the added benefit of collecting the patient's evaluation.[84-86]

Normal skin	**Observer Component**										**Worst scar imaginable**
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	
Vascularization											
Pigmentation											Hypo
											Mix
											Hyper
Thickness											
Relief											
Pliability											
	Patient component										
No, no complaints	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Yes, worst imaginable**
Is the scar painful?											
Is the scar itching?											
No, as normal skin	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Yes, very different**
Is the color of the scar different?											
Is the scar more stiff?											
Is the thickness of the scar different?											
Is the scar irregular											

TABLE 4: PATIENT AND OBSERVER SCAR ASSESSMENT

4. Manchester Scar Scale (MSS)

This scale, proposed by Beausang et al in 1998, includes an overall VAS score added to the individual attribute scores along with POSAS. It evaluates and rates seven parameters viz. scar color, surface, relationship to surrounding skin, margins, size, number and texture. The MSS and VAS ratings are combined to produce an overall scar score, with higher levels indicating clinically worse scars. This information is analyzed, as well as the patient's race, ethnic origin, medical history, etiology of keloid formation, symptoms, therapies, and reactions. In contrast to the VSS, the MSS groups vascularity and pigmentation under the heading of color mismatch in relation to the surrounding skin, allowing for better interpreter agreement. As a result, MSS can be used to examine a larger range of scars, including post-operative scars.[87-90]

Excellent	**Visual Analogue Scale**	**Poor**
Color	Perfect	1
	Slight mismatch	2
	Obvious mismatch	3
	Gross mismatch	4
Matte vs. Shiny	Matte	1
	Shiny	2
Contour	Flush with surrounding skin	1
	Slightly proud/indented	2
	Hypertrophic	3
	Keloid	4
Distortion	None	1
	Mild	2
	Moderate	3
	Severe	4
Texture	Normal	1
	Just palpable	2
	Firm	3
	Hard	4

TABLE 5: MANCHESTER SCAR SCALE

THERAPY

Keloids have been treated using a variety of therapy techniques, with various degrees of effectiveness. Patients seek medical help to correct a cosmetic or functional abnormality, prevent recurrence by surgery or adjuvant pharmaceutical therapy, or relieve physical pain and itching.

There is no single, standardized treatment option that is best for all keloids. The type of therapy employed is determined by the location, size, and depth of the lesion, the patient's age, the existence of comorbidities, and the patient's reaction to previous treatment.

Patients need to be counselled at the onset about the chances of recurrences with each therapeutic option and the possibility of this lesion being more severe than the original keloid.

1. Intralesional steroid injection

Intralesional steroid (ILS), mainly triamcinolone acetonide, is still considered the first line of treatment of keloids. Triamcinolone acetonide is a potent anti-inflammatory hydrocortisone, fluoridated at the ninth carbon.

The mechanism of action involves inhibition of leukocyte and monocyte migration and phagocytosis, vasoconstriction leading to hypoxia and antimitotic effect inhibiting keratinocytes and fibroblast proliferation. It also stimulates fibroblast degeneration and reduce plasma protease inhibitors so that collagenase can degrade collagen. There is an increased growth of basic FGF and decreased in production of TGF-β1, endogenous vascular endothelial growth factor and IGF-I.[48]

Steroids also cause ultrastructural alterations in collagen synthesis, which improve the structure of collagen bundles while causing the keloidal collagen nodules to degenerate.[91-93]

It is injected intralesionally into the upper dermis, typically 0.05ml per linear centimeter of the keloid every 2-6 weeks at a dose ranging from 10mg/ml to 40mg/ml, until clinical resolution or until side effects prohibit use. Fixed needle syringe, lurelog-type or dental syringes with needles not smaller than 27 gauge are used to prevent separation of needle and syringe, when the liquid is forced into the hard mass of the keloid. Care should be taken to inject the lesion itself as it may cause irreversible atrophy of the surrounding skin. The initial injections tend to make the lesions softer and symptom free, but usually does not produce any visible reduction in size or volume.[5]

Ketchum et al[93], also described a dosing schedule based on the age of the patient and size of the lesions:

1. Adults:

   Maximum dose- 120mg. Repeated once a month for 6 months.

   a. 1 to 2 cm^2 lesion- 20-40mg
   b. 2 to 6 cm^2 lesion- 40-80mg
   c. 6 to 10 cm^2 lesion- 80-100mg

2. Children:

   Maximum dose each time as follows -

   a. 1 to 2 years- 20mg

   b. 3 to 5 years- 40mg

   c. 6 to 10 years- 80mg

Intralesional corticosteroid injections had a response rate of 50-100 percent, with a recurrence rate of 9-50 percent.

Adverse effects include pain, skin and subcutaneous fat atrophy, telangiectasia, necrosis, ulcerations and hypo or depigmentation. Systemic side effects like Cushing's syndrome have been infrequently reported in adult and pediatric patients. Pain can be reduced by injecting very slowly or adding lignocaine.[48]

2. 5-Fluorouracil (5-FU)

5-FU is a fluorinated pyrimidine, an antimetabolite, which inhibits thymidylate synthase and interferes with RNA synthesis and function. It has been used to treat keloids and hypertrophic scars successfully since 1989.[94]

In keloids, it blocks collagen synthesis and inhibits fibroblast proliferation. It has an inhibitory effect on TFG-β induced type I collagen gene expression in human fibroblasts.[48]

It is given intralesionally, at a dose of 50mg/ml, 0.05ml per linear centimeter or until blanching appears, at an interval of one or two weeks. The total dose per session ranged from 2-50mg and not beyond 100mg.[31] On an average, 5-10 injections are required to achieve complete flattening of the lesions.[48] Subjective improvement in the form of decrease in pain, pruritus, stretching or pulling sensation and discomfort is first noted, followed by softening and then flattening of lesion.[64]

A study, where intralesional 5-FU (50mg/ml) was administered every week for seven weeks, revealed that 85% of patients experienced greater than 50% improvement and biopsy specimens taken after six injections exhibited reduction in number of hyalinized collagen fibers, regression of nodular concentric arrangement of collagen fibers, less

prominent vascularity, flattening of dermal papillae without any signs of atrophy, pigmentary incontinence, reduction of Ki-67 expression and a slight reduction in TGF-β expression. The recurrence rate after a one year follow up was found to be only 19%.[94]

Adverse effects include pain, swelling, moulting, urticaria, blackish discoloration, superficial ulceration, telangiectasia, purpuras, localized hair loss and minimal systemic absorption.[34,48,94]

3. Hyaluronidase

Hyaluronidase is an enzyme that increases connective tissue permeability by hyaluronic acid hydrolysis. This temporarily reduces the intercellular cement viscosity, promoting diffusion of injected solution, exudates and transudates facilitating absorption and increased bioavailability. It is mainly used in combination with intralesional steroids, to facilitate its absorption in firm or hard keloids. It is available as 1500IU of vacuum dried tablet of ovine origin which is mixed with the desired strength of triamcinolone acetonide and injected into the keloid.[95]

4. Bleomycin

Bleomycin was originally isolated from fungus. Streptomyces verticillus. It has antitumor, antibacterial and antiviral activity as it blocks cell cycle via the inhibition of DNA synthesis, RNA and protein synthesis as well as production of reactive oxygen species.[48,94]

It is thought to reduce collagen synthesis, increase degradation secondary to inhibition of lysyl oxidase which is a cross-linking enzyme involved in the maturation of collagen and TGF-β1 and induce fibroblast apoptosis.

It is administered either as intradermal injections or multiple needle punctures with the help of 22G needles in the form of 40 punctures per 1 cm^2 or 0.1ml (1.5IU/ml) at a maximum dose of 6ml per session. It can be given at monthly or two week intervals. Around two to six sessions may be required for complete flattening of scars.

In a study of 31 keloids, administered intralesionally with bleomycin at one month intervals for three to five sessions, the keloid volumes and functional impairments were significantly reduced with complete regression in 84% of cases.[94]

Caution is required when used in pregnant women and children. Complications such as hyperpigmentation, pain necessitating lidocaine anesthesia, ulceration, Raynaud's phenomenon, gangrene, fibrosis, neutrophilic eccrine hidradenitis, alopecia, edema and nail changes have been reported. It should not be combined with radiotherapy as both emit free radicals. Cutaneous toxicity occurs with doses above 200-300 units and pulmonary fibrosis occurs at doses exceeding 400IU.[94]

Bleomycin is easy to administer, with high regression rate and lesser complications and lower recurrence rate, although cost may be a limiting factor.[31,48]

5. Interferon

Interferons (IFN) are cytokines mainly secreted by T-helper lymphocytes, with anti-proliferative, anti-fibrotic and antiviral properties.

They increase collagen breakdown, interfere with collagen I and III synthesis and cross-linking and increase collagenase production. It also upregulates native p53 and promotes fibroblast apoptosis. TGF-β is also antagonized by systemic interferon therapy.

Although both interferon alpha and gamma were used experimentally in the treatment of keloids, IFN α-2b has a more comprehensive effect on enzymes that modulate collagen levels.[31]

Intralesional injection of IFN α-2b (1.5 million IU) into the wound base and margins twice daily for four days led in a 50% reduction in keloid size in just nine days. To avoid major side effects, the total dose should be kept around 5 million IU.[31,48]

Studies have shown significant benefits over steroid injections with a low recurrence rate of 19%.48 It can also be administered intralesionally in the dosage of 0.01-0.1mg three times a week for three consecutive weeks.[96]

In vitro findings reveal that, interferons work better in young keloids and in keloid prevention than in mature older keloids where the damage is already done.[31]

Unlike other treatment modalities for keloids, interferons produces systemic side effects, such as dose dependent flu-like symptoms (which can be treated with prophylactic and post treatment acetaminophen), headache, pyrexia, arthralgia, fatigue, chills and rarely confusion. Disadvantages also include decreased wound strength, delayed re-epithelialization and pain at the site of injection. It is also considered a high cost therapy.[94]

6. Verapamil

Verapamil is a calcium channel blocker with phenylalkylamines that serves as an antiarrhythmic.

It changes the morphology of fibroblasts (from bipolar to spherical), stimulates procollagenase expression, inhibits extracellular matrix molecule synthesis/secretion (including collagen, glycosaminoglycans, and fibronectin), and enhances collagenase. It also reduces the synthesis of IL-6 and vascular endothelial growth factor in central keloid

fibroblasts, resulting in decreased cell proliferation, increased apoptosis, and increased expression of decorin, a fibroblast proliferation and migration inhibitor.[94]

It is administered intralesionally at a dosage of 2.5mg/ml at three weekly intervals till flattening of lesions or till side effects prevent further use.[97]

Studies revealed that the results of intralesional verapamil were comparable to that of intralesional triamcinolone injection. With the added benefits of being less toxic, less costly and less painful, verapamil can be used as an alternative to triamcinolone injection in the management of keloids.[48]

7. Botulinum Toxin Type A (BTX-A)

BTX-A is an exotoxin released by Clostridium botulinum, which causes flaccid paralysis by inhibiting the release of acetyl choline at the neuromuscular junction.[94]

It causes temporary denervation of smooth muscle fibers, decreasing the tension in the scar. This decrease in tension causes local fibroblasts to gradually change their functional status to proliferate slower, secrete less biologically active markers and synthesize less extracellular matrix and collagen resulting in improvement of keloids. They also reduce TGF-β expression and promote apoptosis. They also reduce substance P, which contributes to improvement of erythema, pain and itching.[98]

It is injected intralesionally into the body of the scar at a dosage of 4U/0.1ml (100 U vacuum-dried powder in a single-use vial for reconstitution diluted in 2 mL of sterile, preservative-free 0.9% saline to constitute a solution) with a 9G needle. It is administered once a month for three months. Several studies showed clinical improvement with respect to size, erythema, itching, pliability and no side effects or recurrences. Minor side effects like itching, pain and allodynia have been reported.[48]

8. Methotrexate

Methotrexate (MTX) is a well-known anti-proliferative and anti-inflammatory medication.

In low doses, its anti-inflammatory effect is mediated by adenosine A2 receptors and by an increase in adenosine release at sites of inflammation.

When combined with excision, MTX has proven quite successful in leading to complete resolution and preventing keloid recurrences. Oral MTX (15–20mg) was given in a single dose every four days, starting a week prior to excision and continuing post-surgery until keloid resolution for three months and prevented keloid recurrence. In two patients, no recurrences were noticed after four years of follow up.

Methotrexate 1ml (10mg with up to a maximum of 2ml being used per dose) and 0.5ml triamcinolone acetonide (20mg) and 1 ml 2% xylocaine can also be given as combination to infiltrate the keloid, at monthly intervals for 6 sessions with good clinical improvement.[99,100]

9. Interleukin-10 (IL-10)

Il-10 is a cytokine that reduces inflammatory responses. IL-10 is necessary for scarless wound repair. It reduces IL-6 and IL-8 secretion which are pro-inflammatory cytokines. Absence of IL-10 leads to an amplified inflammatory response and abnormal collagen deposition.

Injection of IL-10, 48 hours before wounding, has shown to decrease inflammation and decrease expression of pro-inflammatory mediators when compared to controls. At three weeks, the treated wounds showed reduced inflammation, normal dermal architecture and no abnormal collagen deposition.[94]

10. Surgery

Surgical excision is one of the earliest forms of treatment. Surgical excision alone is associated with recurrences in 50-100% of patients, with an exception with earlobe keloids which recur less frequently, provided proper precautions and postoperative treatment is followed.[101] Excision surgery is thought to trigger more collagen synthesis, resulting in faster growth and bigger keloids.[34]

Excisional surgery is thought to trigger more collagen synthesis, resulting in faster growth and bigger keloids. Following guidelines helps prevent recurrences:

I. Intradermal and subcuticular sutures are preferred to avoid suture marks.
II. Monofilamentous suture material is preferred over braided sutures to minimize local inflammatory reaction.
III. To avoid the creation of dead space and haematoma, any stuck hair or sinus tracts must be removed with minimal tissue stress.
IV. Sutures need to closed with least amount of tension.
V. Sutures should be removed as early as possible.
VI. Tissue expanders may be used as the pressure of the expander may beneficially alter collagen production pre-operatively.
VII. If primary closure is insufficient, flap advancement, autograft, or composite allograft might be used to close the lesion.[31,102,103]

Various surgical procedures for keloid removal are available[96]:

A. <u>Excisional Surgery</u>

Keloids with a narrow attachment to the skin, or those that are small and linear, can be completely removed with a little margin of skin around them. Sutures are placed parallel to the skin tension lines to close the incision. To lower the rate of recurrence, adjuvants

such as radiotherapy, intralesional steroid, or 5-FU should be administered (55-80 percent). Recurrence rates may also be reduced with postoperative pressure therapy.[34]

B. Excision with Autografting

Small to medium-sized keloids are removed, leaving a rim of keloid tissue behind that works as a splint to keep the central tensile contraction from becoming excessive. The overlaying epidermis is removed and used as an autograft, which is sutured along the base's periphery. There is no need for a separate donor site, which has the extra benefit of preventing the creation of another keloid and relieving tension on the overlaying skin, which has already been stretched by the keloid.[48]

C. Excision with auto flap (keloid fillet flap)

A semicircular incision is made near the keloid's base, with one side remaining attached. As a flap (fillet flap), the skin (epidermis and portion of the dermis) is removed from the keloid mass and reflected back, revealing the keloid tissue. The keloidal mass is then completely excised or debulked, and the reflected flap is sutured back to the base all the way around. This surgical method works well for large earlobe keloids.[48]

D. Keloid core extirpation

The inner fibrous core is excised and the defect is covered by a keloid rind flap, which was arterialized by the subcapsular vascular plexus.[48]

11. Radio surgery

It is a form of excision of keloid using a modified electrosurgical device that uses radio waves. The lateral heat damage is minimal. They are mainly useful in treating midline keloids on the chest that have trapped hair and sebum, which gets repeatedly

infected. The keloid is slit open and the lesion is debulked using various loop probes. The wound is then allowed to heal by secondary intention.

Advantages over cold steel excision is that it is simpler to perform, minimum or no bleeding, no donor site required reducing the occurrence of a donor site keloid and all tracks are opened out releasing trapped hair, sebum and debris.

Disadvantages are prolonged healing time, cost, wound heals by secondary intention, hence no atrophic scar is formed and long term follow up is required.[96]

12. Radiotherapy

Radiation therapy can be used as monotherapy or as an adjunctive to surgical excision. A combination of surgery followed 24 hours by radiotherapy is thought to be the most effective approach for the management of keloids, which cause significant morbidity/limitation of joint movement/contracture, with a recurrence rate varying from 9 to 72%.

Superficial X-rays, electron beam therapy, strontium-90 brachytherapy and 32p-patch contact brachy radiotherapy have been used in the management of keloids. Of the various modes, electron beam therapy is the most effective in prevention of recurrent keloids. It reaches the border of the papillary layer and the reticular dermis, where the keloid is generated, whereas the soft X-rays cannot reach to that level.

Radiation damages the fibroblasts directly, affecting the structure and organization of collagen. Vascular hyperplasia is also reduced. In vitro studies show that keloid fibroblasts have a higher rate of apoptosis than normal fibroblasts, re-establishing cell population balance.

The dosage is 20Gy in four fractions over four days on anterior chest wall, scapular region and suprapubic region and 10Gy in two fractions over two days on the earlobes. Other sites, the dose is 15Gy in three fractions over three days.

Keloids resulting from burns show poorer outcomes than those resulting from surgery or trauma. Due to the possibility of radiation induced malignancies, it is avoided over the breast and thyroid (exclusively papillary carcinoma) regions. It is contraindicated in pregnancy and in pediatric patients, where growth plates need to be shielded to prevent growth retardation. Complications include dyschromias, alopecia, telangiectasia, cigarette-paper atrophy and skin peeling.[31,48,64,101]

13. Silicone material

Silicone is available in the form of creams, gels, sheets, silastic sheets and orthosis garments. Silicone gel sheets (SGS) are soft, adherent, semi occlusive covering material, fabricated from cross-linked polydimethyl siloxane polymer, 3- 5mm in thickness.

Although its mechanism is incompletely understood, it is suggested that silicone under occlusion affects hydration of the skin by decreasing the water vapor transmission rate, which is responsible for decrease in capillary permeability, reduced hyperemia and collagen deposition. Hydration and the static electricity that develops at gel dressing and skin interface also affects the keratinocytes of the lesion to alter growth factor secretion which affects the fibroblasts. Temperature mediated activation of collagen breakdown may also be involved.

The sheet may result in flattening of the lesion, increased malleability and softening of the scar. They also reduce the symptoms associated with these keloids, the erythema and cause lightening of the lesions.

These silicone dressings are secured with micropore over the keloids, for 12 hours a day for a span of 3-6 months. They are washed with soap and water when it becomes dirty and replaced when it cracks, crumbles or wear off. It has resulted in a moderate improvement in 50% of the cases, in various studies. Silipos gel are firmer and made from silicone and mineral oil. They last longer than SGS (6 months or more). This method is preferably used as a preventive method immediate postoperatively, once the wound has healed. They can be combined with pressure dressings to further enhance the reduction in size of keloids.

Advantages of silicone products are the ease of administration and being noninvasive without significant side effects.

Skin maceration, erosion, redness, and pruritus are all side effects that go away after removing the gel for a few days and then reapplying it in a few patients. Although silicone gel is pleasant to use, it requires active patient cooperation and long-term use.[31,48,64,101]

14. Pressure therapy

Pressure therapy has been popular for treatment and prevention of raised scars, especially earlobe keloids, for many decades.

Topical pressure probably acts by the following mechanisms:

a. Decreased blood flow with decrease in α2 macroglobulin and hence causing increased collagenase mediated collagen breakdown.
b. Lower level of chondroitin sulphate and decreased activity of MMP-28 with increased collagen degradation.
c. Decreased scar hydration, mast cell stabilization with decreased neovascularization and extracellular matrix production.

d. Partial occlusion of microcirculation leading to hypoxia resulting in fibroblast degeneration and collagen degradation. Loose linear collagen bundles are laid down with increased space and decreased cellularity.

The pressure should be over the inherent capillary pressure of 25mm of Hg, but should not exceed 40mm of Hg, which will cause reduction in peripheral blood circulation. This pressure will alleviate itching and pain and cause early scar maturation.

Earlobe earrings, custom made suits, individual moulds that are held with Velcro straps are available, which are held in place for 12-23 hours for at least 6-12 months. Pressure can be stopped when the discontinuation does not result in swelling of the affected area. They are quite successful in reducing keloid recurrence rates post operatively.

Side effects include pressure loss of custom made garments, discomfort from heat and swelling, swelling of limbs, rashes, eczema, excessive friction, blistering, break down of scar and reduced compliance of patients.[31,34, 48,64,96,101]

15. Laser

Argon laser was the first laser used, but was discontinued due to its poor response rate.

a. <u>Carbon dioxide (CO2) laser</u>

It was used in small to medium sized keloids, by doing a saucer shaped shave excision. The radiation emitted is absorbed by the intracellular and extracellular water, which produces instant vaporization by heating target tissue to 1000C. It has a few technical advantages over cold steel excision such as increased speed, coagulation of small vessels, ability to seal off small nerve endings thereby minimizing discomfort, less trauma and minimum inflammation and limited thermal spread causing little peripheral tissue necrosis. It is however not recommended as monotherapy any more due to a high recurrence rate of 90% or more.[34]

b. Neodymium-doped: Yttrium Aluminium Garnet (Nd:YAG) 1064nm continuous wave laser

It causes infarction and sloughing of the keloid surface, with selective bio inhibition of collagen synthesis and softening and size reduction of the lesion. However, due to its absorption by melanin pigment in the epidermis, the dermal penetration and action is limited. The recurrence rate was found to be 53-100%.[34]

c. Pulsed Dye Laser (PDL)

Of all, PDL proved to be the most effective in the improvement of scar texture, redness, size, reduction in itching, pain and pliability. The wavelengths of 585nm and 595nm are most frequently used with pulse duration of 0.45ms and a fluence of 6.5-7.25J/cm^2. They are repeated every 6- 8 weeks for at least 6 months. They work better on early keloids as the target chromophore is hemoglobin. They decrease the microvasculature leading to anoxia, causing reduced cellular function. Following cytokine activation, laser-induced heating causes disulphide band breakdown, followed by fiber remodeling or collagenolysis. They also reduce TGF-β1 induction and upregulation of MMP expression in keloid tissue leading to their regression. Mature keloids are not helped by PDL. Another study showed a 57-83% improvement with 585nm flash pump PDL in sternotomy scars. They work better on combination with steroid or interferon injection or CO2 laser.[34,96,101]

d. Other lasers and light based treatments

Intense Pulsed Light (IPL), LED phototherapy and Photodynamic therapy have also been found to be quite efficacious in the management of keloids.[104]

e. Laser-assisted drug delivery (LADD)

Lasers have been used to increase drug penetration beyond the stratum corneum so as to increase the bioavailability of topical scar therapies. The common ablative lasers, such as CO_2 and Er: YAG lasers, are applied to create cylindrical zones of micro ablation, into the skin which allow for topical agents to reach the dermis. The common topical keloid-treating agents, such as corticosteroids, 5-FU, and imiquimod have been used, however there is limited literature investigating the use of LADD for keloid treatment.

Topical imiquimod and 5-FU with LADD has shown to increase drug penetration and decrease the required dosage for optimal efficacy in animal skin models. Further studies are necessary to explore the effectiveness of these topical therapies with LADD for keloid treatment.[34]

16. Cryosurgery

Cryosurgery with liquid nitrogen (LN_2) is an extremely useful modality to treat keloids either as a monotherapy or in combination with intralesional steroid or 5-FU injections. Its efficacy for treating keloids vary from 50-80%.[34]

LN_2 achieves destruction of keloid scars through direct cell anoxia in the lethal zone (-220C) due the formation of intracellular crystals, which then removes water from the cells and thereby decreases the density of fibrous tissue. In addition, the cold temperature damages the endothelial cell junctions and causes blood stasis, thereby producing microthrombi, vascular injury and ultimately tissue necrosis and sloughing. Histologically, the treated scars have reduced myofibroblasts and mast cells and more organized and parallel collagen fibers.

Various techniques of cryotherapy have been adopted:

a. **Spray technique**: They are useful for small to medium sized keloids. Most authors propose a 30 second freeze time, repeated 2-3 times per cycle. Here, the lethal zone involves the surface epithelium leading to more skin damage and the deeper pathological tissue in the dermis may be spared. Most keloids require around 20 sessions, repeated monthly. Side effects include pain, hypopigmentation especially in dark skinned individuals and prolonged healing phase of more than one month.

b. **Cryoroller technique**: They are used in flat surfaced, extensive keloids. It causes superficial epidermal peeling along with dermal remodeling, leading to complete flattening and faster resolution.

c. **Intralesional cryosurgery**: It is useful in treating large and bulky keloids. Following universal sterile precautions and adequate local anesthesia with lidocaine 1% and epinephrine, an 18G hypodermic needle, spinal needle or cryoprobe is inserted into the keloid scar by gradual twisting method till it penetrates to the opposite end. LN2 is then passed through the needle till the keloid is visibly frozen from one end to the other, which typically takes 10 to 60 minutes depending on scar volume. After allowing the scar to thaw for a few minutes, the needle is gently removed and the site is dressed with an antibiotic ointment and sterile gauze. Prophylactic antibiotics and anti-inflammatory agents are prescribed for 8-10 days. In this technique, a 3600 lethal zone is created, which directly destroys the pathological cells and minimally damages the surface epithelium. The typical clinical course is initial peripheral erythema followed by edema, bulla formation, exudation, crust formation and subsequent healing with a flat, mildly atrophic scar within 2- 3weeks.

Studies have showed an average of 51% reduction in scar volume following a single session and significant improvement in pain, itching, hardness and color. Side effects include infection, sloughing, transient hypo/depigmentation (about which the patients need to be thoroughly counselled prior to treatment), transient hyperpigmentation, atrophy and scarring. [48,94,96,105]

17. Retinoids

Vitamin A and its equivalents are used topically and intralesionally to promote fresh wound healing and the regression of problematic scar tissue.

They reduce fibroblast growth while increasing epidermal proliferation, allowing the healing process to return to normal. They may improve chronic inflammation and prevent expansion of keloid tissues into normal skin. They are potent inhibitors of MMPs and they upregulate MMP13 while downregulate MMP 1 and 8 in keloid derived fibroblasts at both mRNA and protein levels. They also inhibit TGF-β1 induced type 1 collagen gene expression in human fibroblasts. They also suppress sebum production, which is known to play a role in keloid pathogenesis.

Topical 0.05% tretinoin is applied locally for 12 weeks. A significant reduction in weight and size was observed in a few studies, especially when combined with intralesional steroid injections.

Adverse effects include photosensitivity, skin irritation and slight skin atrophy.[41,48,100]

18. Imiquimod 5% and resiquimod cream

Imidazolquinolones are topical immunomodulators that are toll-like receptors (TLR) 7 and 8 agonists.

They induce production of cytokines, including TNF and interferons alpha and gamma (IFN-α and IFN-γ) which has antifibrotic activities and inhibit collagen production. They alter the expression of an apoptotic gene and thereby has antikeloidal effect.[34]

Imiquimod is applied at night for five days a week and continued for 8 weeks. They are usually used as an adjunct to surgical therapy to prevent keloid recurrence, to be applied four to six weeks after surgery. Resquimod is 10-100 fold more potent than imiquimod.

Common side effects are itching, burning, pain, blister/ulceration, localized hyperpigmentation and flu-like symptoms-fever, headache, nausea, fatigue, muscle pain and bone pain.[48,100]

19. Onion extract and Heparin

Topical preparations containing onion extract have been used for many years to treat wounds and keloids. They have antioxidant and anti-inflammatory properties and prevent fibroblast proliferation.

When used as adjunctive therapy along with monthly intralesional steroid injections, pain sensitiveness, itching and elevation improved but erythema and induration did not. Combination of onion extract and silicone gel sheet was found to be more effective. The gel is applied thrice daily for at least three months.[31,48]

20. Antihistamine

Histamine H1 blockers are anti-inflammatory and antiproliferative drugs that have been proven to reduce collagen deposition and synthesis in keloidal fibroblasts by inhibiting the release of TGF-β1 from the cells. The prevention of mast cell degranulation and histamine release has also been observed to relieve the burning sensation, discomfort, and

pruritus associated with keloids. Tranilast, at a dosage of 3-300μM, inhibits collagen synthesis of fibroblasts and TGF-β1 in keloid.[48,100]

21. Penicillamine, β-Aminipropionitrile and Colchicine

Penicillamines and -Aminipropionitrile are lysyl oxidase inhibitors that prevent collagen from crosslinking, rendering it more sensitive to collagenase action. They're taken orally in tandem with colchicine, which boosts collagenase activity. This method manipulates extracellular enzymes to change the collagen turnover ratio. After 18 months, there have been no recurrences and no side effects have been observed.[41]

22. Pentoxyphylline

Few studies have showed that pentoxyphylline was found to inhibit fibroblasts and collagen, glycosaminoglycans and fibronectin activity, but has no effect on collagenase activity.[48]

23. Collagenase D

Intralesional injection of Collagenase D, derived from Dermestes frischii, resulted in temporary reduction in scar volume, returning to same or greater level after 6 months of follow-up. [48]

24. Catechins

Epicatechin gallate resulted in improvement in quality of scar formation in a rat incisional wound model.[48]

25. Mitomycin C

Mitomycin C is an antineoplastic antibiotic with antiproliferative effects on fibroblasts through DNA synthesis inhibition. It can cause fibroblast arrest without sacrificing re-epithelialization.

In a study where mitomycin C (1mg/mL) was applied on wound beds for three minutes after keloid resection and repeated after three weeks, 4 out of 10 patients were pleased with the treatment outcome, only one was disappointed, and approximately 80 percent were satisfied with the outcome.

On the contrary, in a study using patients as their own controls, Sanders et al reported that topical mitomycin C applied to excised keloids made no difference in keloid recurrence. The mixed results of the mentioned trials may be related to small study sample sizes, short-term follow up, different applied doses of mitomycin C, different application regimens, and a lack of strict randomization.[34]

No adverse reaction to the mitomycin C has been reported.[100]

26. Tamoxifen citrate

Tamoxifen citrate is a selective estrogen receptor modulator (SERM) used in the treatment of breast cancer. Tamoxifen may lead to improved wound healing in keloids by decreasing the expression of TGF-β1. It also inhibits the proliferation of keloid fibroblasts and decreases the rate of collagen synthesis through RNA transcription alteration, cell G1 phase delay or arrest, and insulin growth factor (IGF) suppression.

Topical tamoxifen citrate chemical treatment has been shown to improve scarring.[100]

27. Calcineurin inhibitors

Tacrolimus (FK-506) is a potent immunosuppressor that binds to the receptor FKBP. It inhibits calcineurin and suppresses production of IL-2. In a study, on treating patients with tacrolimus 0.1% ointment twice daily for 12 weeks, a decrease in induration, tenderness, erythema, and pruritus was seen.[100]

28. Sirolimus

The mammalian target of rapamycin (mTOR) is a serine/threonine kinase, which plays an important role in the regulation of metabolic processes and translation rates.

Reports have shown mTOR to be a regulator of collagen expression and its inhibition induces a decrease in extracellular matrix (ECM) deposition. Sirolimus inhibits mTOR, blocks response to IL-2, and decreases ECM deposition. Increased expression of the gli-1 oncogene is present in keloids, and sirolimus inhibits gli-1 signal transduction, which may restore the natural apoptosis process with decreased proliferation of the ECM. Secreted VEGF expression has shown to be downregulated in a dose-dependent manner in the presence of sirolimus in co-cultured keloid keratinocyte and fibroblast. Therefore, sirolimus may inhibit VEGF and may control the expression profile of underlying dermal fibroblasts.[100]

29. Vascular endothelial growth factor (VEGF)

VEGF is important in the promotion of neovascularization and cell growth in both normal and pathological wound healing. It serves as an endothelial cell mitogen, increases vascular hyperpermeability, and promotes deposition of an extravascular fibrin matrix.

The use of short interfering ribonucleic acid (siRNA) sequences for the inhibition of the VEGF gene represents a potential therapeutic strategy for keloids.[100]

30. Basic fibroblast growth factor

Basic fibroblast growth factor (bFGF) promotes the growth and differentiation of many cell types. It has both angiogenic and mitotic properties, influencing tissue remodeling, wound healing, neovascularization, and promoting tumor growth.

bFGF has been found to significantly inhibit the differentiation of mesodermal progenitor cells into myofibroblasts, which are the key mediators of tissue fibrosis and the primary producer of collagen. It also accelerates wound healing and improves scar quality by regulating the extracellular matrix production and degradation.

Patients receive either low-dose dermal injections (0.1µg/m per wound), high dose injections (1µg/m per wound) or a rinse with high-dose bFGF (1µg/m wound). The amount of scarring is found to be lower in 6-12 months, post-operation. No adverse events were observed.

bFGF represents an important tool for the future treatment of keloids and scarring.[100]

31. Hepatocyte growth factor

Hepatocyte growth factor (HGF) is a cytokine that has regenerative, angiogenic, antiapoptotic and antifibrotic properties. It has been found to alter the levels of cytokines, such as VEGF and TGF-β1, and, therefore, may play a role in the prevention of scar formation. They are administered intradermally to incisional wounds to enhance the healing process with less noticeable scarring. Further clinical trials examining the therapeutic uses of this cytokine are warranted.[100]

32. Mannose 6 phosphate

Mannose-6-phosphate (M6P) surface receptors are involved in the proteolytic activation of TGF-β. When injected into wounds, M6P competes with latent M6P for the M6P receptors, inhibiting TGF-β1 and β2 activation, which can lead to reduced fibrosis. A phase I dose-escalation trial found M6P to be safe and well tolerated and found that it accelerated epithelialization significantly. Current trials are further exploring the role of M6P in the acceleration of wound healing and testing two dose levels and two routes of administration (intradermally and topically).[100]

33. Transforming growth factor beta

Avotermin, human recombinant TGF-β3, has been studied in several Phase 2, double-blind, placebo-controlled, randomized, controlled trials (RCTs) showing that the intradermal injection given at or immediately after surgery was safe and produced a statistically significant improvement in scar appearance. Postsurgical injections of antisense TGF-β1 oligonucleotides, which are associated with a reduction in the expression of the TGF-β1 gene, have demonstrated to be effective and have obtained long-lasting inhibition of TGF-β-mediated scarring. Further studies are needed to elucidate their role in treatment of keloids.[100]

COMBINATION THERAPIES

Combination therapies are, at present, the most effective management for keloids.

Surgery along with steroids

Surgical excision followed by a monthly intralesional injection of triamcinolone acetonide (10 mg/ml) into the wound bed has proven to be quite efficient in preventing recurrences. There have been reports of cure rates exceeding 80%. The side effects are similar to those seen with steroid treatment alone, and they are temporary.[91-93,105]

Carbon dioxide lasers with steroids

Excision of keloids with CO2 lasers followed by intralesional injection of steroids have showed comparable results to those of surgical excision with steroid injection with the added benefit of lesser post-operative pain.[106-108]

Surgery plus radiation

Excision of keloid followed by immediate radiotherapy can be used in areas without any underlying visceral structures. This combination yields a cure rate of 65- 99%, with minimal side effects of occasional pigment change and ulceration. They are however, avoided in pregnant women and pediatric patients.[41]

Surgery with compression earrings

Excision of earlobe keloid followed by the use of compression earrings leads in cure rates of more than 80% with little adverse effects.[109,110]

Surgery with silicone gel sheeting

Excision of keloid with SGS for up to 24 hours a day for 4-6 months results in recurrence-free rates of more than 80%. Minor skin irritation and maceration are among the side effects. Patient compliance is another issue that arises frequently.[111-113]

Surgery plus 5-FU

Injection of 5-FU into wound beds following surgical excision of the keloid has shown to yield better results with fewer recurrence rate than surgery alone. Adverse effects like skin irritation is also minimal.[114]

Surgery with imiquimod

Following surgical excision, application of 5% imiquimod cream to the suture line and surrounding skin every night for 8 weeks showed no recurrences after 24 weeks of follow-up. Itching, burning, discomfort, and blisters were among the side effects observed.[115]

Cryosurgery with intralesional steroids

Cryotherapy causes edema in the tissue, which allows steroid to enter more easily, enhancing the keloid's reaction to treatment. In a study, cryosurgery alone resulted in complete keloid flattening in 51% of instances, but when combined with steroid injections, response rates increased to 84 percent.[116-118]

5-FU with steroid injection

It was found that addition of triamcinolone acetonide (0.1ml of 10mg/ml) to 0.9ml of 5-FU, improved both efficacy and decreased the pain of injection.[31]

Intralesional injection of triple medicine combination of steroid, 5-FU and hyaluronidase

Combining injectable 5-FU (50mg/ml) (an antimetabolite that suppresses fibroblast production), triamcinolone acetonide (40mg/ml) (an anti-inflammatory agent) and hyaluronidase (1500IU) (enzyme that dissolves the fibrous bands) showed faster resolution with a low side effect profile and good cosmetic results.[119]

PREVENTION

When it comes to keloids, prevention is crucial, as current treatment guidelines are often not completely successful.

Patients with a family history of keloids should avoid ear piercings, cosmetic procedures or elective surgeries. If required, ear piercings may be done in early childhood.

Following surgery, wounds need to closed with minimal tension along Langer's lines. Pressure garments may be used for 4-6 months after injury. Skin grafts, tissue expanders and healing by second intention may be considered. Preventative intralesional steroid may be administered during the procedure and regularly thereafter. Intralesional interferons and radiotherapy can also be considered.

Similarly, dark skinned individuals with a family history of keloids, presenting with varicella or herpes zoster need to be aggressively treated with antivirals.

Acne patients with keloidal tendencies need to be closely monitored and treated. They should be educated to present at the first sign of an inflammatory acne lesion for intralesional corticosteroids. Multiple lesions are an indication for oral antibiotics or a trial of isotretinoin.

Adequate debridement of contaminated wounds, good hemostasis, gentle handling of tissues and limited foreign bodies are other precautions to be considered. Adequate nutrition is required so that normal tissue substrates can be efficiently synthesized.[31,48]

FUTURE THERAPEUTIC AGENTS

Several potential treatments that are still in experimental phase include[120]:

1. Hydroquinone or bleaching agents:

   It has been noted that albinos (mostly kids) do not develop keloids and vitiligo often causes regression of underlying keloid. Hence, hydroquinone and other bleaching agents may be tried in treating keloids. They are best used within the first five months of keloid formation. Combining surgical excision with application of the agents over the excised site plus 1-2cm margin has also been tried.[120]

2. Glucose 6 Phosphate dehydrogenase (G6PD):

   Keloids have been found to be more common in patients with G6PD deficiency. As a result, an agent that can reduce or block G6PD could be effective in the treatment of keloids.[120]

3. Hyperbaric Oxygen:

   Hypoxia activates fibroblasts, but excessive oxygen tension may inhibit them. The response of fibroblasts to high and low oxygen tension is compared in studies.[120]

FUTURE RESEARCH

Keloids have several characteristics of malignancy- poor regulation of growth, proliferation beyond the boundaries of the initial insult and increased collagen synthesis. This points to future advances in keloid therapy lying in the direction of an immunological approach rather than the slash and burn approach we now pursue. Time will tell if interferons or other immune response modifiers will be the magic wand to treat keloids.[31]

MATERIAL & METHODS

METHODOLOGY

Source of data:

This study was conducted in outpatient clinic of Dermatology, Venereology and Leprosy in R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar from December 2019 and May 2021 in patients with keloids. This was a hospital based interventional study.

Study Design:

Randomized Control Study

Sample size calculation:

Sample size was estimated based on the median improvement percentile of 68.8% based on study by Emad et al; expecting an improvement of 30% better outcome in the new treatment modality with 90% power and alpha error of 5%, estimated sample size of the group is 77 and including 10% dropout rate and compensating for the loss by adding 8 more subjects, the final sample size was estimated to be 85 in each group.

Inclusion criteria:

1. All patients above 12 years from either gender, attending the outpatient department and diagnosed with keloid were included in the study.
2. Patients consenting for the study and were willing for follow up.

Exclusion criteria:

1. Infected keloids.
2. Co-existing inflammatory skin diseases, like psoriasis, lichen planus, eczema, etc.

3. Patients with unrealistic expectations or with psychiatric illnesses.
4. Pre-existing bleeding disorders, renal diseases, hepatic disease
5. Lactating and pregnant women were excluded.
6. Patients with immunodeficiency diseases.
7. Diseases that react adversely to cold (Raynaud's disease, cryoglobulinemia, cold urticaria).
8. Wound healing abnormalities.

Method of Data Collection:

- The study will comprise of patients of either gender, above the age of 12 years, having single or multiple keloids of size not more than 10 cm in the largest diameter.
- The patients were randomly divided into two groups, which were administered two different treatment regimens.
- Before starting therapy, a full physical and systemic examination was performed, as well as any necessary fundamental investigations, such as a complete hemogram, BT/CT/APTT, blood sugar, liver function test, renal function test, HIV 1 and 2, HbsAg, VDRL, and any other relevant inquiry.
- Serial photographs of the keloids were taken before the start of therapy and subsequent visits, during the course of treatment.
- The information collected in clinical history included patient's age and sex, address, occupation, site of lesion, number of lesions, duration of lesions, family history of keloids, previous treatment taken and associated symptoms such as pain, pruritus, cosmetic disfigurement, skin discoloration and restriction of movement of the affected site.

- An informed consent was obtained from each patient after explaining the nature of the disease, course and prognosis.
- They were also counselled about the need for consistent and prolonged treatment and the possibility of recurrence of the keloid.
- The institutional ethics committee granted permission to perform the study.

Group 1

Following universal sterile precautions, the patient will be given cryotherapy with liquid nitrogen until the appearance of a 1mm halo of freeze, which will usually take around 10-20 seconds, at every session. Intralesional corticosteroids will be given to the keloid after the second thaw.

Corticosteroid injections with Triamcinolone 40mg/1ml strength will be given. The volume differs among the patients due to the varying sizes of the keloids. We will use 0.1ml per cm^2, but will not exceed 1ml per lesion. The patient is given treatment once a month for 4 months, till lesions have flattened or a maximum of 4 treatment sessions, whichever was sooner.

The drug is loaded in 1 cc syringe and injected under aseptic precautions with 26 Gauge needle. Multiple injections of 0.1 ml or > 0.1ml are given regular intervals, and response is assessed by the Manchester scar scale.

Group 2

Following universal sterile precautions, a topical anaesthetic cream (lignocaine 2.5% w/w + prilocaine 2.5% w/w) will be applied on the lesion 1 hour before the procedure following which, one session of ablative fractional CO_2 laser will be given in each sitting. A topical corticosteroid (betamethasone cream) will be applied over the keloid after laser

treatment. Patient will also be advised to use topical betamethasone cream twice a day, starting on the day of procedure till the end of the treatment. The patient is given treatment once a month for 4 months, till lesions have flattened or a maximum of 4 treatment sessions, whichever was sooner.

- At the end of each session, all patients were assessed for improvement and any side effects.
- If the required therapeutic response was reached before completing four therapy sessions, the treatment was ended.
- Throughout the study, patients gave information about the effects and adverse effects of their treatment.
- Photographs were taken on day one of treatment and in subsequent visits till completion of treatment.
- In all patients, the improvement was judged based on regression in size as well as the flattening of the lesion and improvement of symptoms

Statistical Analysis:

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test or Fischer's exact test** (for 2x2 tables only) was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. **Independent t test** was used as test of significance to identify the mean difference between two quantitative variables.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs.

P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

GROUP 1:-ILS Triamcinolone with Cryotherapy

GROUP 2:-Fractional CO2 LASER with Topical Betamethasone

Sample size calculation:

Sample size was estimated based on the median improvement percentile of 68.8% based on study by Emad et al; expecting an improvement of 30% better outcome in the new treatment modality with 90% power and alpha error of 5%, estimated sample size of the group is 77 and including 10% dropout rate and compensating for the loss by adding 8 more subjects, the final sample size comes out to be 85 in each group.

$$\text{Sample size} = \frac{Z_{1-\alpha/2}{}^2 p(1-p)}{d^2}$$

Here

$Z_{1-\alpha/2}$ = Is standard normal variate (at 5% type 1 error ($P<0.05$) it is 1.96 and at 1% type 1 error ($P<0.01$) it is 2.58). As in majority of studies P values are considered significant below 0.05 hence 1.96 is used in formula.

p = Expected proportion in population based on previous studies or pilot studies.

d = Absolute error or precision – Has to be decided by researcher.

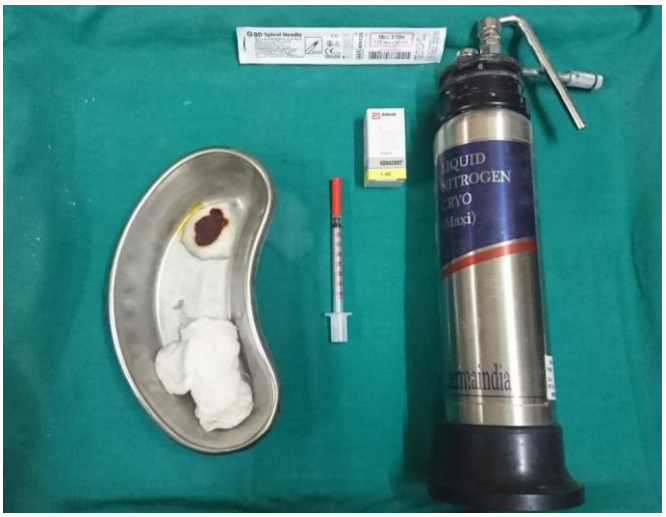
Sample Size: 85 in each group. Total = 170

Evaluation

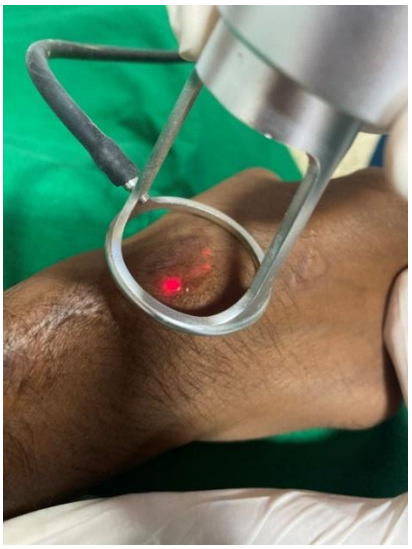
All the subjects underwent a maximum of 4 treatment sessions, or lesser if the lesions get flattened prior to 4 treatment sessions.

All treatment sessions were performed by a single skilled dermatologist. Keloid status throughout the treatment and follow-up period was assessed by serial photographs under similar lighting conditions. Blinded scoring of pre- and post-treatment photographs was done by Manchester Scar Scale (MSS) with regards to changes in color, finish, contour, distortion, texture.

Pain scoring of the patient was also assessed during the treatment sessions.



PHOTOGRAPH 1: Cryogun with triamcinolone acetonide (40mg/ml) and insulin syringe for cryotherapy with intralesional steroid injection.



PHOTOGRAPH 2: Fractional CO2 Laser being performed over a keloid

RESULTS

RESULTS

A comparative study between two treatment regimens in a total of 170 patients of clinically diagnosed cases of keloid was conducted. Patients were randomly divided in two groups of 85 each, each group undergoing one regimen. Regimen I was Cryotherapy with Intralesional triamcinolone acetonide (40mg/ml) injection. Regimen II was Fractional CO2 LASER with Topical Betamethasone.

AGE	GROUP		TOTAL
	1	2	
<20yrs	13	12	25
	15.3%	14.1%	14.7%
21-30yrs	17	26	43
	20.0%	30.6%	25.3%
31-40yrs	25	29	54
	29.4%	34.1%	31.8%
41-50yrs	26	14	40
	30.6%	16.5%	23.5%
>50yrs	4	4	8
	4.7%	4.7%	4.7%
Total	85	85	170
	100.0%	100.0%	100.0%

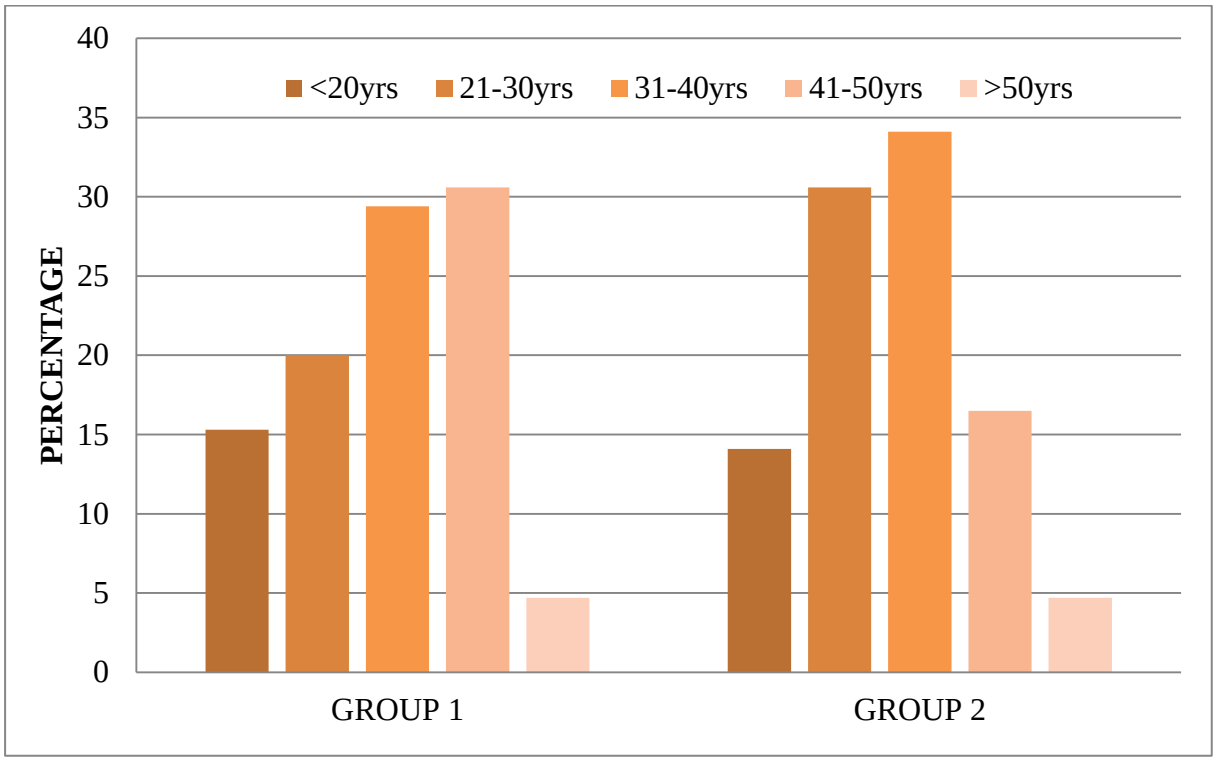
TABLE 6: - DISTRIBUTION OF SUBJECTS ACCORDING TO AGE GROUP BETWEEN GROUPS

Amongst the subjects in both the groups, majority (31.8%) were in the age range of 31-40 years followed 25.3% subjects in 21-30 years age-group.

Among subjects in Group 1, 30.6%of the subjects were in 41-50yrs age group followed by

29.4% of the subjects were in 31- 40yrs age group, 20.0% of the subjects were in 21-30yrs age group, 15.3% of the subjects were <20 years of age and 4.7% of the subjects were above 50 years of age. Among subjects in Group 2, 34.1% of the subjects were in 31-40yrs age group followed by 30.6% of the subjects were in 21-30yrs age group,16.5% of the subjects were in 41-50yrs age group, 14.1% of the subjects were <20 years of age and 4.7% of the subjects were above 50 years of age.

P value was found to be 0.213, and there was no statistically significant difference found between both the groups with respect age.



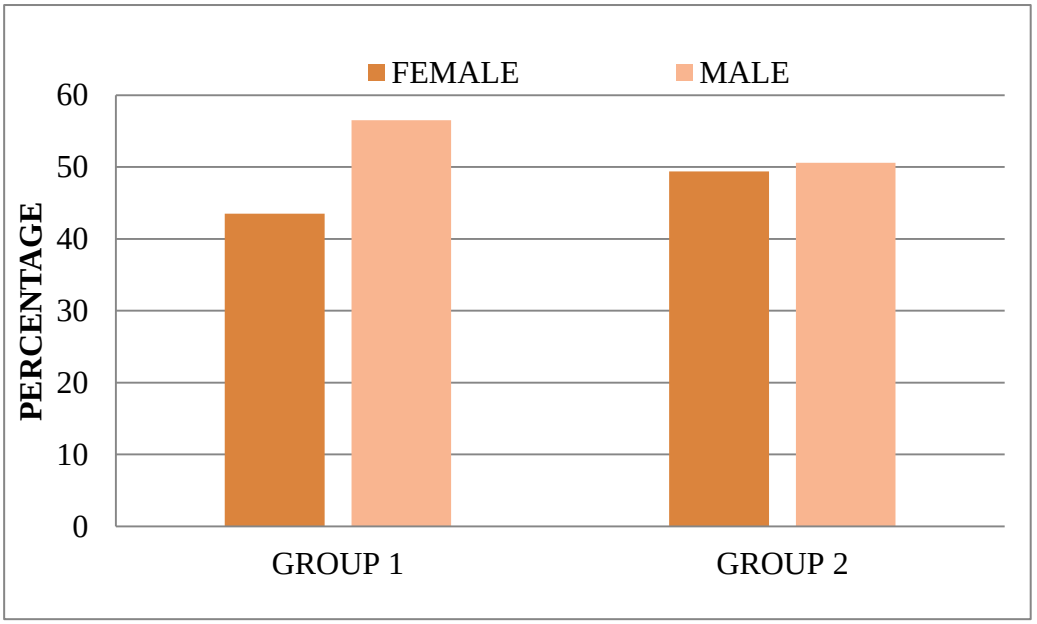
GRAPH 1: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO AGE GROUP BETWEEN BOTH GROUPS

GENDER	GROUP		TOTAL
	1	2	
Female	37	42	79
	43.5%	49.4%	46.5%
Male	48	43	91
	56.5%	50.6%	53.5%
Total	85	85	170
	100.0%	100.0%	100.0%

TABLE 7: - DISTRIBUTION OF SUBJECTS ACCORDING TO GENDER BETWEEN GROUPS

Among subjects in Group 1, 43.5% of the subjects were female and 56.5% of the subjects were male. Among subjects in Group 2, 49.4% of the subjects were female and 50.6% of the subjects were male.

P value was found to be 0.539, and there was no statistically significant difference found between groups with respect to gender of the subjects.



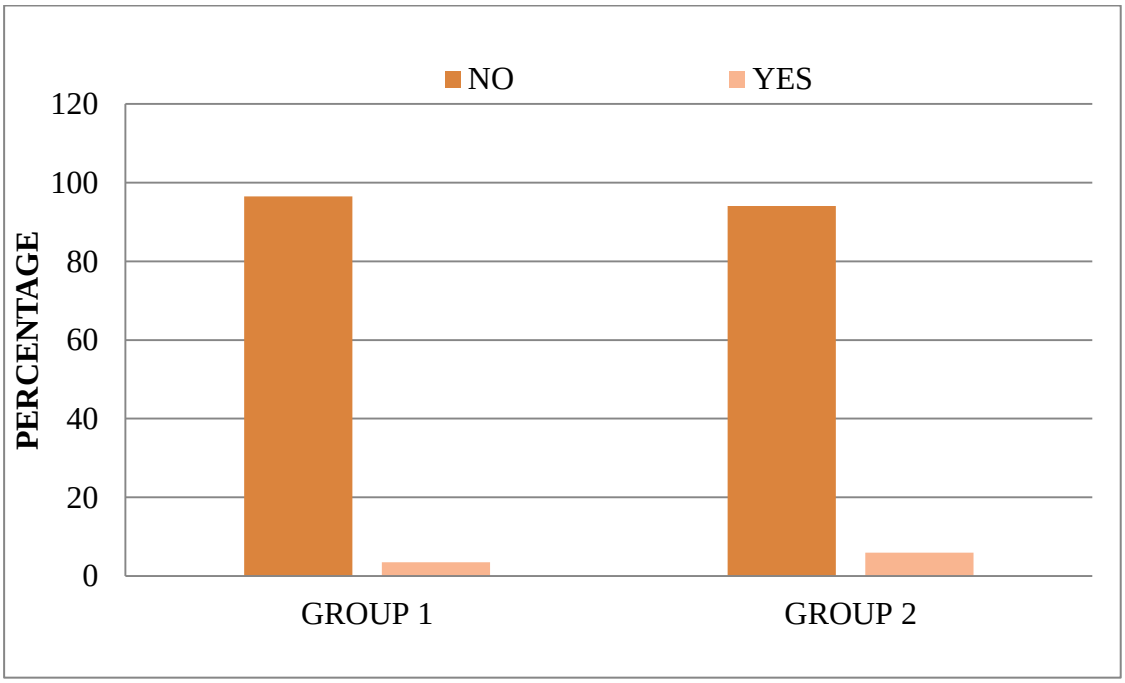
GRAPH 2: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO GENDER BETWEEN GROUPS

FAMILY HISTORY	GROUP		TOTAL
	1	2	
No	82	80	162
	96.5%	94.1%	95.3%
Yes	3	5	8
	3.5%	5.9%	4.7%
Total	85	85	170
	100.0%	100.0%	100.0%

TABLE 8: - DISTRIBUTION OF SUBJECTS ACCORDING TO FAMILY HISTORY BETWEEN GROUPS

Majority (95.3%) of the patients had no family history of keloids and only 4.7% of the cases gave a positive family history. Of those with a positive family history, only 1 (12.5%) patient developed multiple keloids.

P value was found to be 0.720, and there was no statistically significant difference found between groups with respect to the family history.



GRAPH 3: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO FAMILY HISTORY BETWEEN GROUPS

OCCUPATION	GROUP		TOTAL
	1	2	
Skilled	17	11	28
	20.0%	12.9%	16.5%
Semiskilled	25	33	58
	29.4%	38.8%	34.1%
Unskilled	43	41	84
	50.6%	48.2%	49.4%
Total	85	85	170
	100.0%	100.0%	100.0%

TABLE 9: - DISTRIBUTION OF SUBJECTS ACCORDING TO OCCUPATION BETWEEN GROUPS

Among the occupational groups, unskilled workers especially housewives, farmers and factory workers constituted majority (49.4%) of treatment seekers, followed by semi-skilled workers constituting 34.1% of patients and 16.5% were skilled workers.

P value was found to be 0.289, and there was no statistically significant difference found between groups with respect occupation.

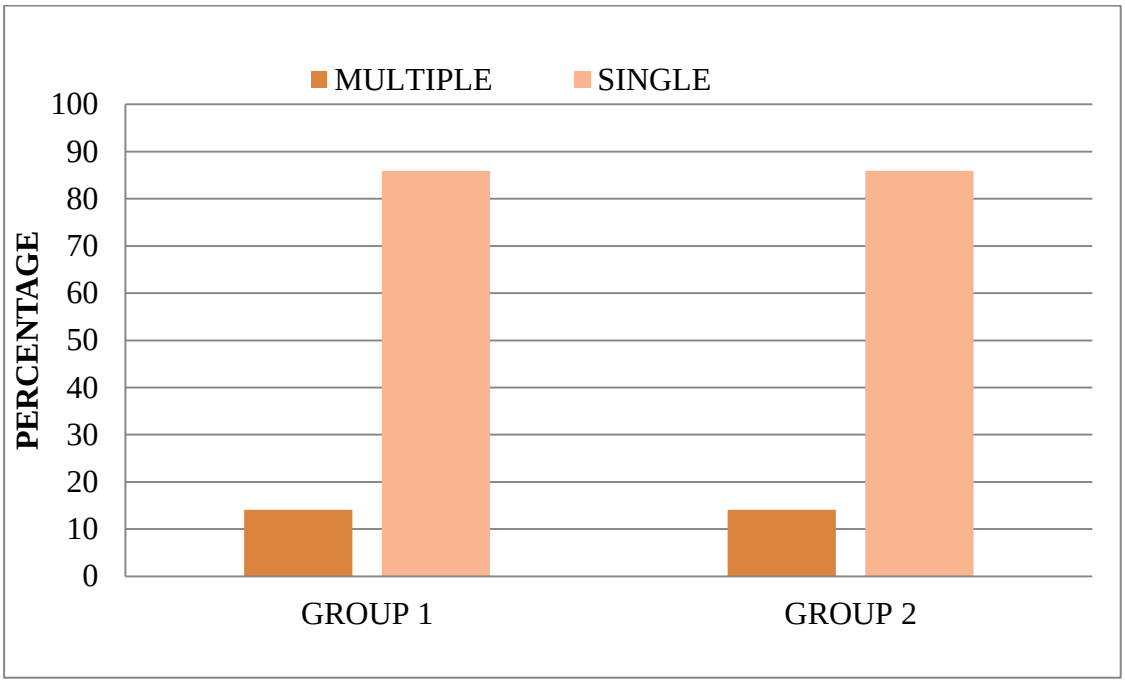
GRAPH 4: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO OCCUPATION BETWEEN GROUPS

NUMBER OF KELOIDS	GROUP		TOTAL
	1	2	
Multiple	12	12	24
	14.1%	14.1%	14.1%
Single	73	73	146
	85.9%	85.9%	85.9%
Total	85	85	170
	100.0%	100.0%	100.0%

TABLE 10: - DISTRIBUTION OF SUBJECTS ACCORDING TO NUMBER OF KELOIDS BETWEEN GROUPS

In our study, majority (85.9%) of patients presented with only one keloid and 14.1% of patients presented with more than 2 keloids.

P value was found to be 1.00, and there was no statistically significant difference found between groups with respect number of keloids



GRAPH 5: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO NUMBER OF KELOIDS BETWEEN GROUPS

SITE	GROUP 1	GROUP 2	TOTAL
MID STERNUM	29(34.1%)	33(38.8%)	36.45%
EAR LOBE	22(25.8%)	17(20%)	22.9%
ARM	14(16.4%)	12(14.1%)	15.3%
SHOULDER	20(23.5%)	21(24.75%	24.1%
LEGS	6(7.05%)	12(14.11%)	10.6%
OTHERS	11(12.9%)	17(20%)	11.1%

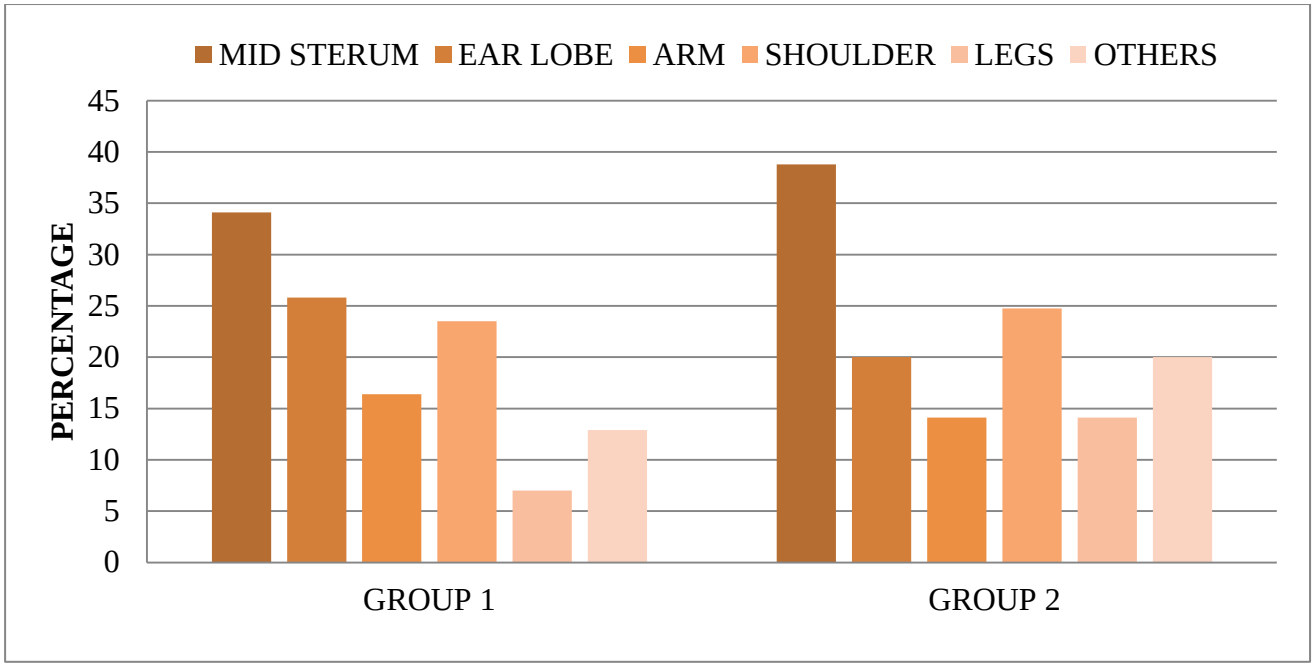
TABLE 11: - DISTRIBUTION OF SUBJECTS ACCORDING TO SITE OF KELOIDS BETWEEN GROUPS

In this study, keloids were most commonly found on the mid-sternum (36.45%), followed by shoulder (24.1%), earlobe (22.9%), upper extremity (15.3%) and lower extremity (6.2%). 11.1% patients had keloids on other parts of the body. While keloids may be found anywhere on the body, they have a predilection for certain sites such as chest, shoulders, back, upper limbs and ears.[5]

According to a study by Berman et al[1], the most frequently involved sites were chest, shoulders, head and neck areas (mainly the earlobes), arms and upper back.

Muir et al[123], also found a higher incidence of keloids over the presternal area followed by deltoid and ear. Bayat et al[124] also observed that keloids occur most commonly over the chest, shoulder, upper back, nape of neck and ear lobes.

The results of the present study are in agreement with those of the above-mentioned studies.



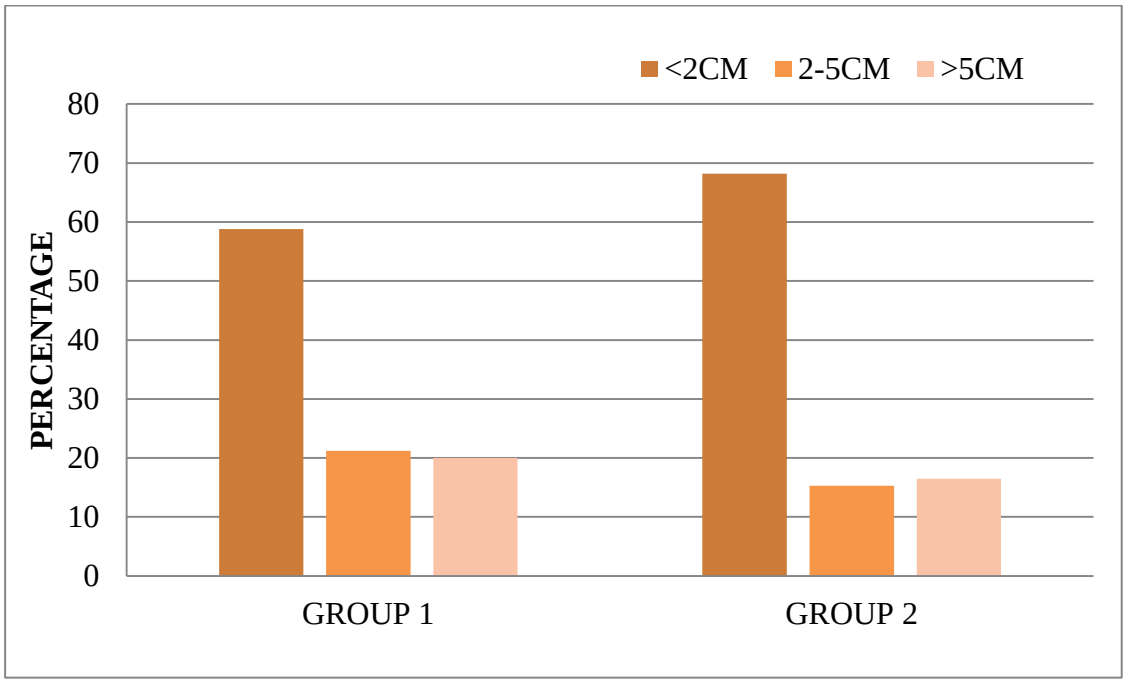
GRAPH 6: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO SITE OF KELOIDS BETWEEN GROUPS

SIZE	GROUP		Total
	1	2	
<2cm	50	58	108
	58.8%	68.2%	63.5%
2-5cm	18	13	31
	21.2%	15.3%	18.2%
>5cm	17	14	31
	20.0%	16.5%	18.2%

TABLE 12: - DISTRIBUTION OF SUBJECTS ACCORDING TO SIZE OF KELOIDS BETWEEN GROUPS

Majority (63.5%) of patients had keloids measuring <2 cm in the largest diameter, followed by 18.2% patients who had keloids measuring between 2-5 cm and 18.2% patients for whom the keloids measured >5cm.

P value was found to be 0.430, and there was no statistically significant difference found between groups with respect size of keloids.

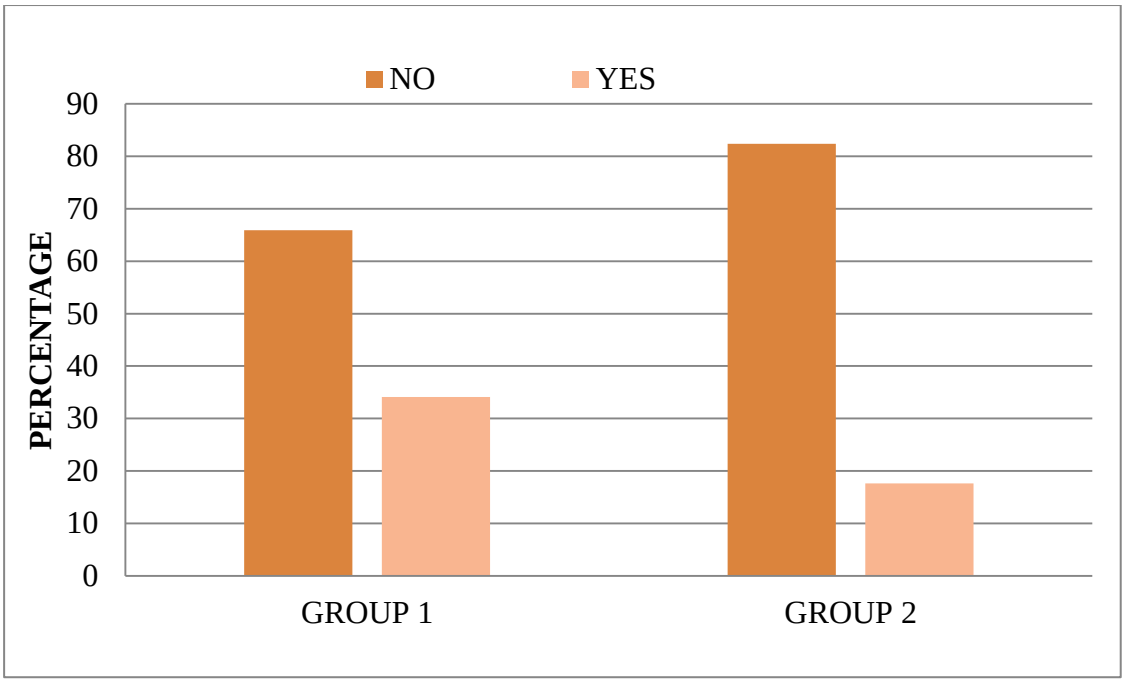


GRAPH 7: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO SIZE OF KELOIDS BETWEEN GROUPS

PRURITUS	GROUP		TOTAL
	1	2	
No	56	70	126
	65.9%	82.4%	74.1%
Yes	29	15	44
	34.1%	17.6%	25.9%
Total	85	85	170
	100.0%	100.0%	100.0%

TABLE 13: - DISTRIBUTION OF SUBJECTS ACCORDING TO PRURITUS BETWEEN GROUPS

25.9% of all patients complained of pruritus while for 74.1% of them, the keloid was asymptomatic.



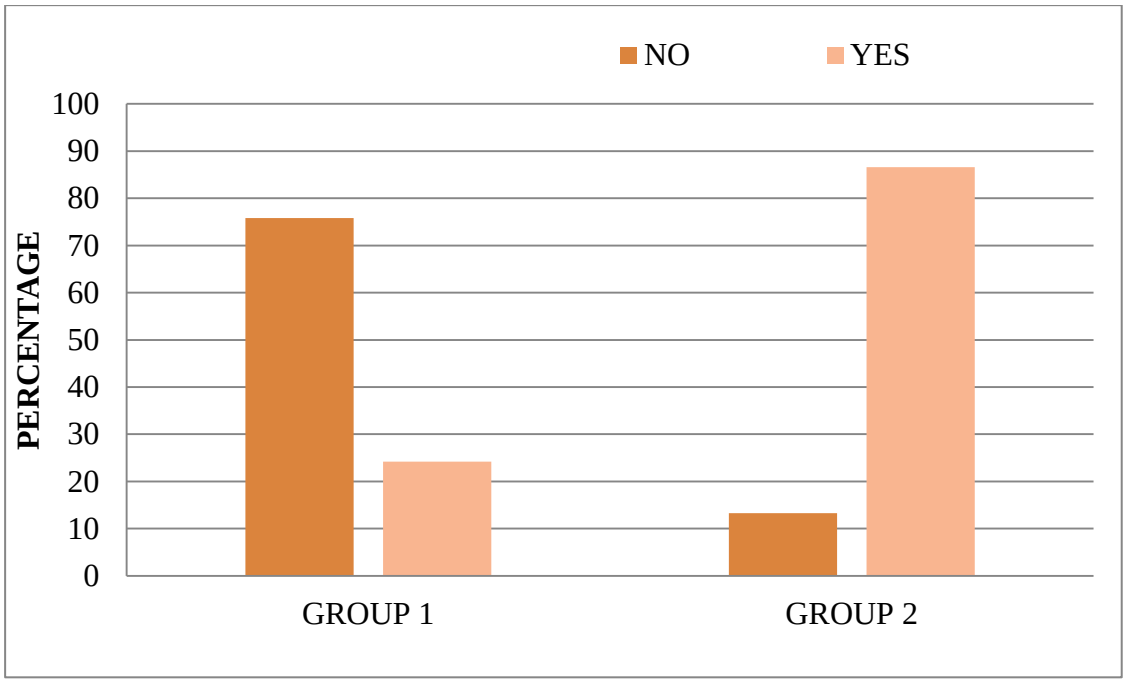
GRAPH 8: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO PRURITUS BETWEEN GROUPS

IMPROVEMENT IN PRURITUS	GROUP	
	1	2
No	7	2
	24.2%	13.3%
Yes	22	13
	75.8%	86.6%
Total	29	15
	100%	100%

TABLE 14: - DISTRIBUTION OF SUBJECTS ACCORDING TO IMPROVEMENT IN PRURITUS AFTER TREATMENT BETWEEN GROUPS

Of the patients complaining of pruritus, 79.5% had improvement (reduction) in pruritus after treatment.

P value was 0.709, and there was no statistically significant difference found between groups with respect improvement in pruritus after treatment.



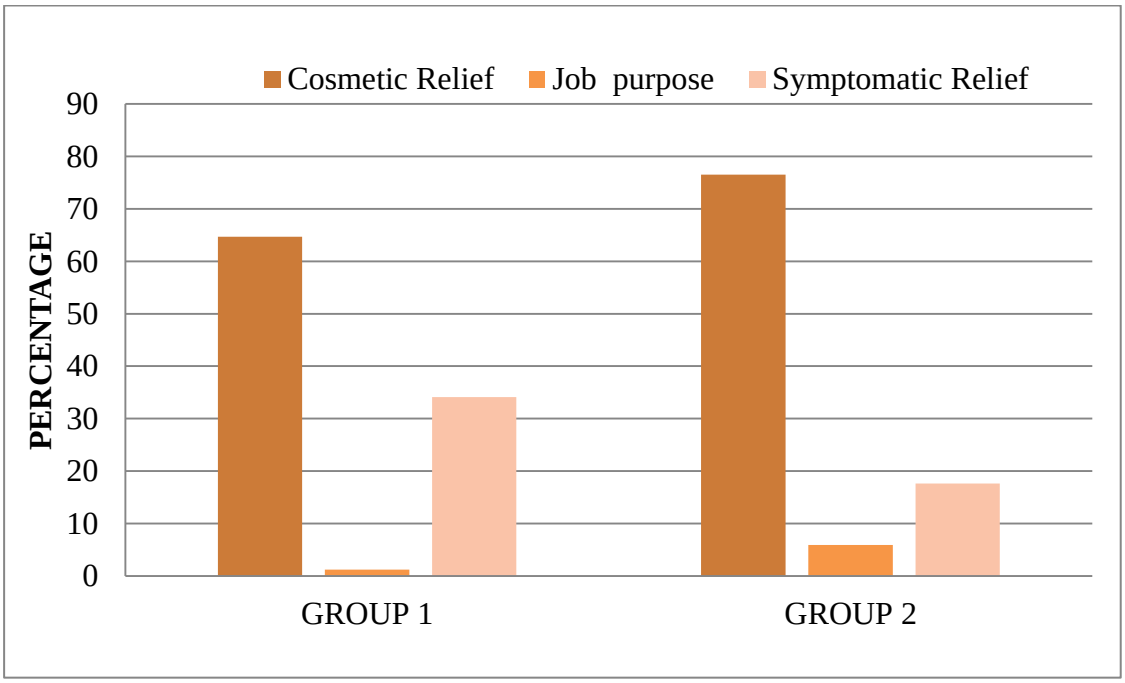
GRAPH 9: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO IMPROVEMENT IN PRURITUS AFTER TREATMENT BETWEEN GROUPS

REASON FOR TREATMENT	GROUP		TOTAL
	1	2	
Cosmetic Relief	55	65	120
	64.7%	76.5%	70.6%
Job purpose	1	5	6
	1.2%	5.9%	3.5%
Symptomatic Relief	29	15	44
	34.1%	17.6%	25.9%

TABLE 15: - DISTRIBUTION OF SUBJECTS ACCORDING TO REASON FOR TREATMENT BETWEEN GROUPS

Majority (70.6%) of the patients sought medical intervention for cosmetic reasons, followed by 25.9% of patients who came for treatment for symptomatic relief. Treatment for job purposes comprised of 3.5% of treatment seekers.

P value was found to be 0.019, showing statistically significant difference found between groups with respect to reason for treatment.



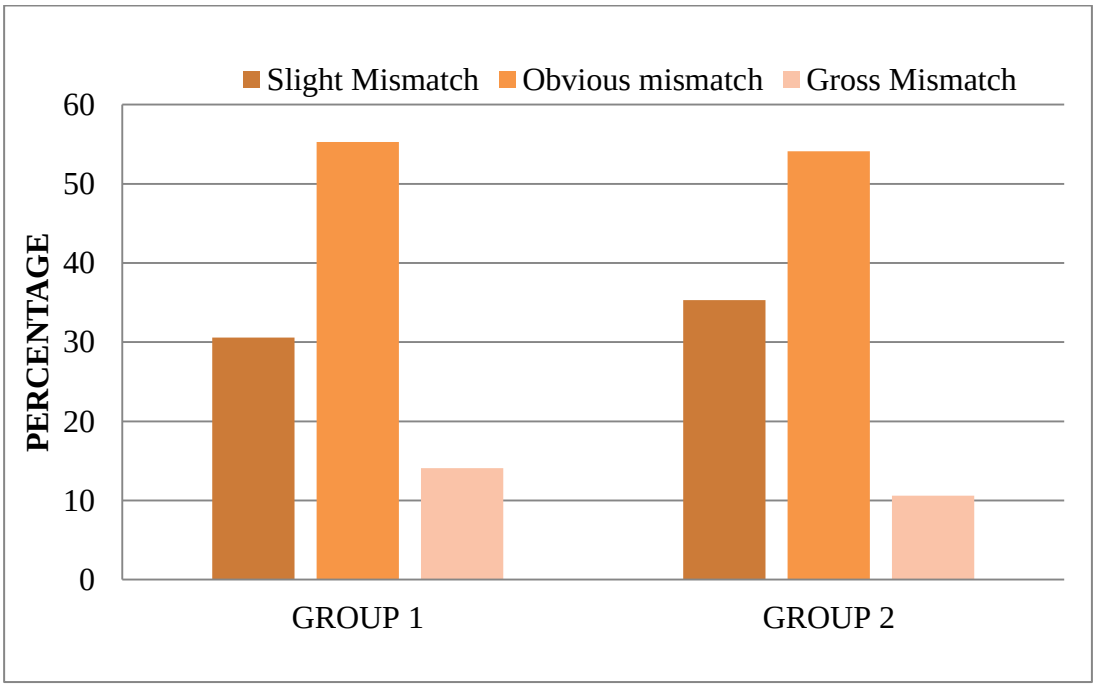
GRAPH 10: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO REASON FOR TREATMENT BETWEEN GROUPS

COLOR BEFORE TREATMENT	GROUP		TOTAL
	1	2	
Slight mismatch	26	30	56
	30.6%	35.3%	32.9%
Obvious mismatch	47	46	93
	55.3%	54.1%	54.7%
Gross mismatch	12	9	21
	14.1%	10.6%	12.4%

TABLE 16: - DISTRIBUTION OF SUBJECTS ACCORDING TO COLOR BEFORE TREATMENT BETWEEN GROUPS

54.7% of patients had obvious mismatch of color of keloid with the surrounding skin, followed by 32.9% patients who had slight mismatch. 12.4% of patients however had gross mismatch of color with the surrounding skin.

P value was found to be 0.696, showing no statistically significant difference found between groups with respect to color.



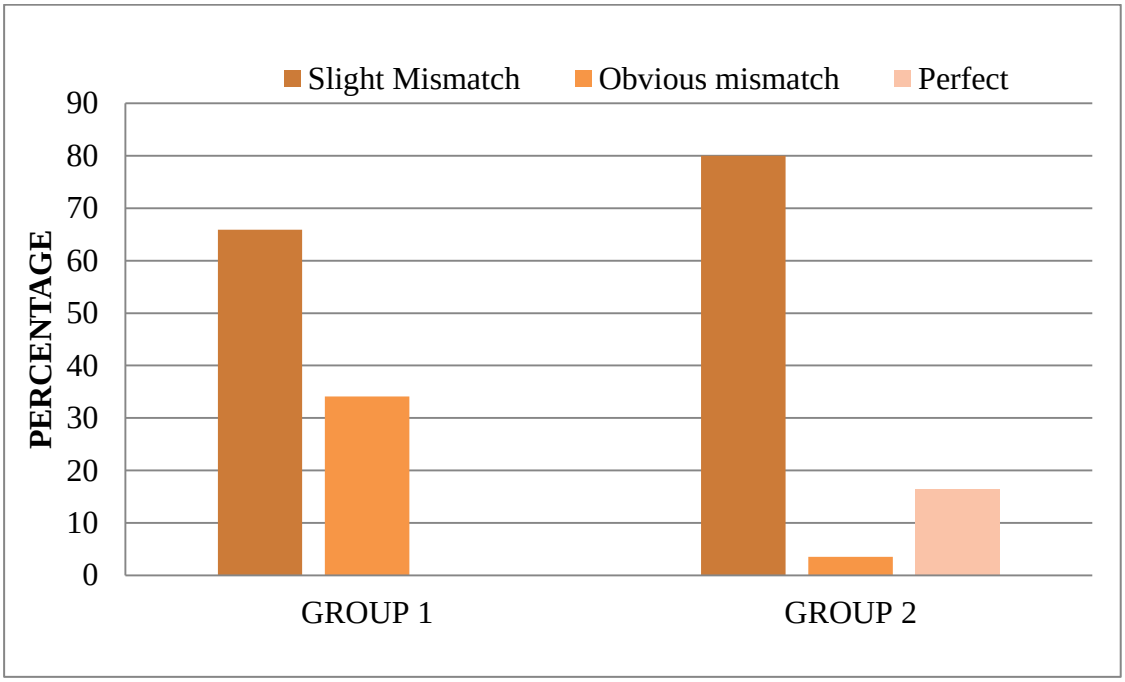
GRAPH 11a: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO COLOR OF KELOID BEFORE TREATMENT BETWEEN GROUPS

COLOR AFTER TREATMENT	GROUP		TOTAL
	1	2	
Perfect	0	14	14
	.0%	16.5%	8.2%
Slight mismatch	56	68	124
	65.9%	80.0%	72.9%
Obvious mismatch	29	3	32
	34.1%	3.5%	18.8%

TABLE 17: - DISTRIBUTION OF SUBJECTS ACCORDING TO COLOR OF KELOID AFTER TREATMENT BETWEEN GROUPS

Following treatment, majority (72.9%) of patients just had slight mismatch of color with the surrounding skin. However, 34.1% patients in group 1 continued to have obvious match of color. It was also noted that 16.5% of subjects in group 2 had perfect color match with the surrounding skin, providing better cosmetic relief to the patient.

P value was <0.001, showing a statistically significant difference found between groups with respect color of keloid after treatment.



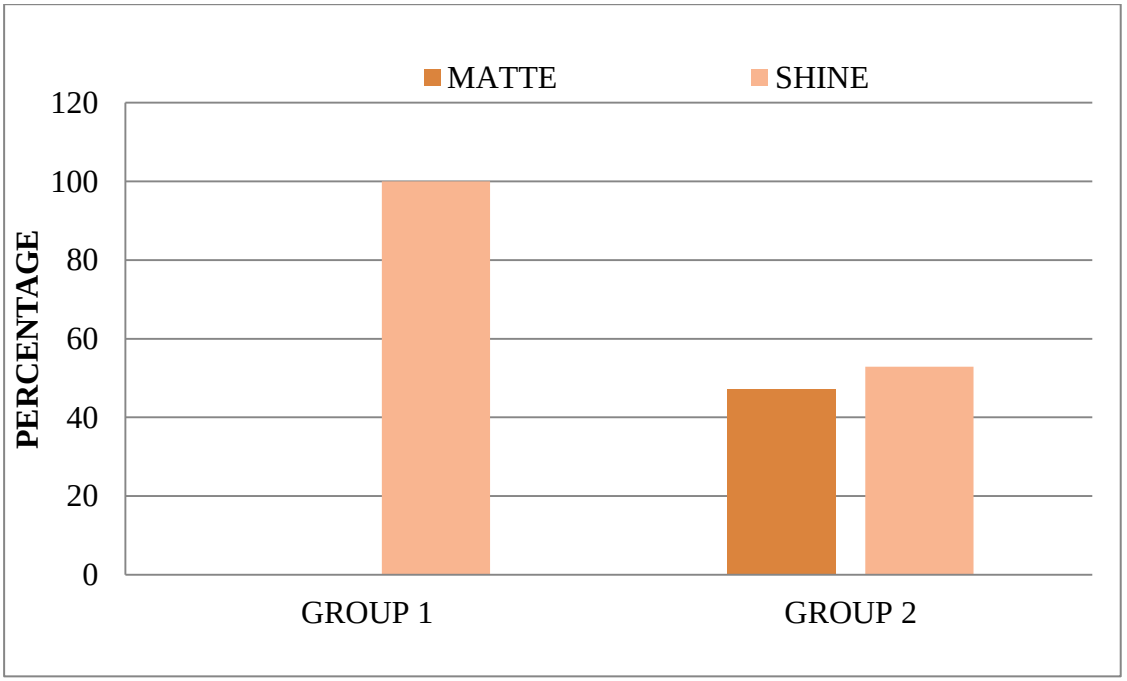
GRAPH 11b: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO COLOR OF KELOID AFTER TREATMENT BETWEEN GROUPS

FINISH AFTER TREATMENT	GROUP		TOTAL
	1	2	
Matte	0	40	40
	0%	47.1%	23.5%
Shine	85	45	130
	100.0%	52.9%	76.5%

TABLE 18- DISTRIBUTION OF SUBJECTS ACCORDING TO FINISH AFTER TREATMENT BETWEEN GROUPS

Keloids in subjects of both the groups had shiny finish prior to treatment. After receiving the treatment, 47.1% of subjects in group 2 had improvement in the finish of the keloid. However, none of the patient in group 1 had the improvement.

P value was <0.001, which was statistically significant difference found between both groups with respect to finish.



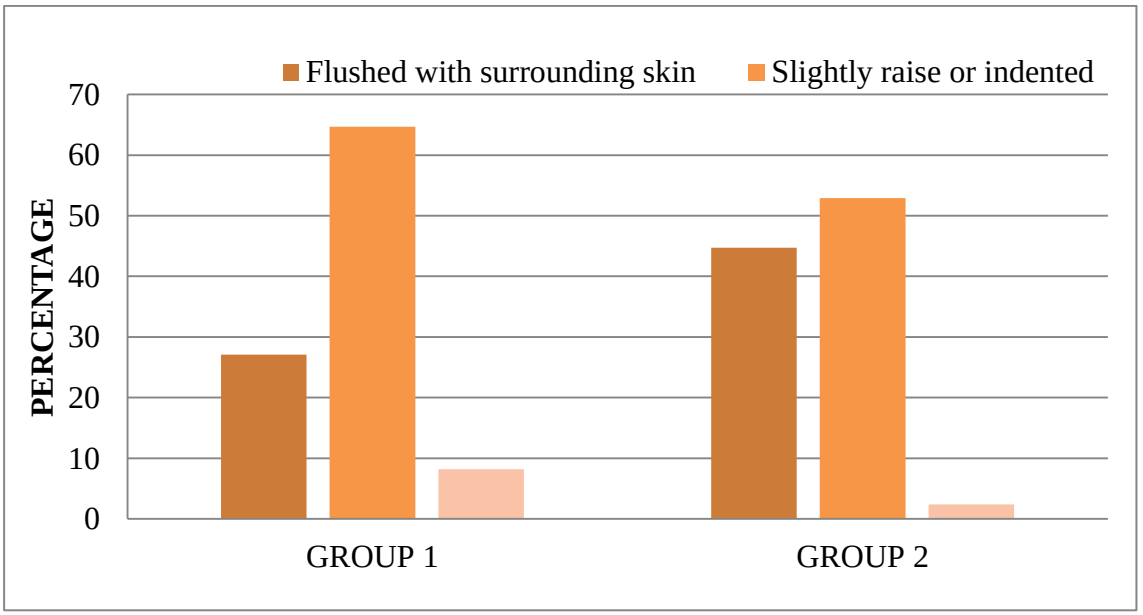
GRAPH 12: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO FINISH AFTER TREATMENT BETWEEN GROUPS

CONTOUR AFTER TREATMENT	GROUP	
	1	2
Flushed with surrounding skin	23	38
	27.1%	44.7%
Slightly raised or indented	55	45
	64.7%	52.9%
Hypertrophic	7	2
	8.2%	2.4%

TABLE 19- DISTRIBUTION OF SUBJECTS ACCORDING TO CONTOUR AFTER TREATMENT BETWEEN GROUPS

In both the groups, the contour before treatment was keloid in all the subjects. After receiving treatment, majority (58.8%) subjects had slightly raised or indented contour. 35.9% of subjects had flushing with the surrounding skin, but it was seen more in patients in group 2 than group 1. A very small proportion (5.3%) of subjects had hypertrophic contour of the keloid after treatment.

P value was 0.023, which was a statistically significant difference found between groups with respect to contour.



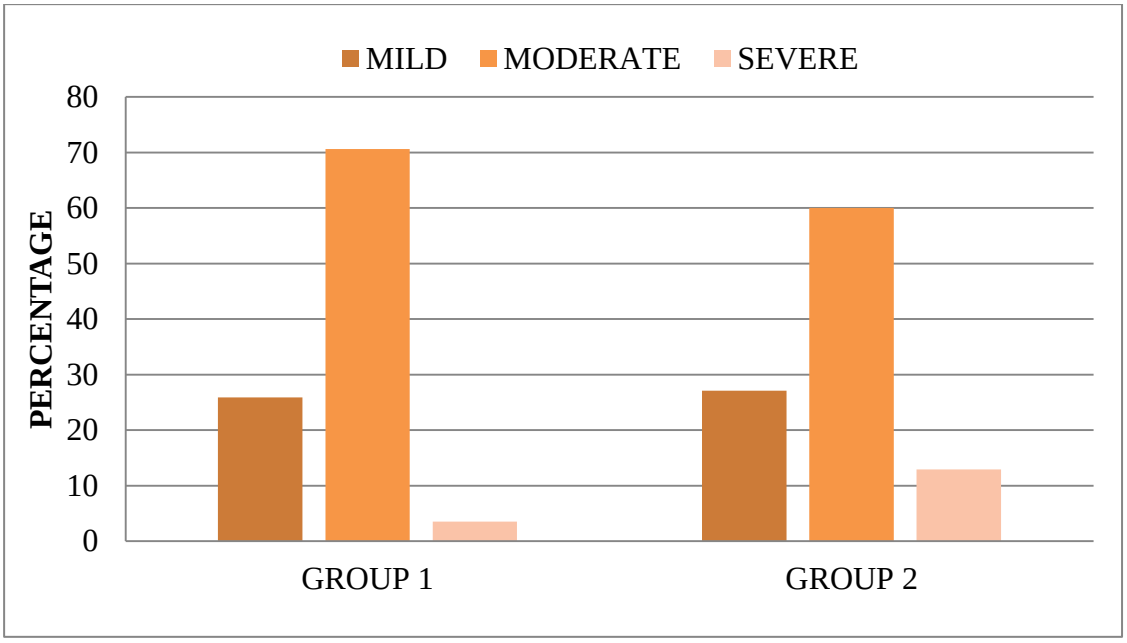
GRAPH 13: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO CONTOUR OF KELOID AFTER TREATMENT BETWEEN GROUPS.

DISTORTION BEFORE TREATMENT	GROUP		TOTAL
	1	2	
Mild	22	23	45
	25.9%	27.1%	26.5%
Moderate	60	51	111
	70.6%	60.0%	65.3%
Severe	3	11	14
	3.5%	12.9%	8.2%

TABLE 20- DISTRIBUTION OF SUBJECTS ACCORDING TO DISTORTION BEFORE TREATMENT BETWEEN GROUPS

65.3% subjects had moderate distortion, followed by 26.5% subjects who had mild distortion. A small proportion (8.2%) of subjects had severe distortion.

P value was found to be 0.070, which was not statistically significant between groups with respect to distortion.



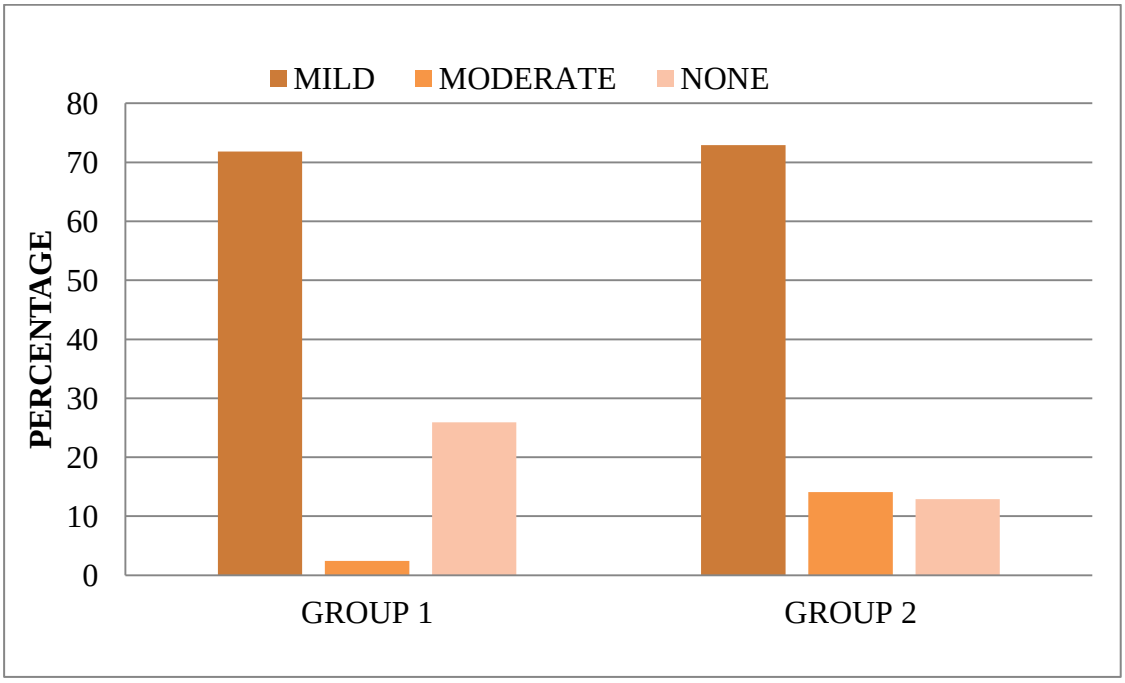
GRAPH 14a: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO DISTORTION BEFORE TREATMENT BETWEEN GROUPS

DISTORTION AFTER TREATMENT	GROUP		TOTAL
	1	2	
None	22	11	33
	25.9%	12.9%	19.4%
Mild	61	62	123
	71.8%	72.9%	72.4%
Moderate	2	12	14
	2.4%	14.1%	8.2%

TABLE 21- DISTRIBUTION OF SUBJECTS ACCORDING TO DISTORTION AFTER TREATMENT BETWEEN GROUPS

Majority (72.4%) subjects had mild distortion after treatment. 19.4% of subjects had no distortion while 8.2% had moderate distortion.

P value was found to be 0.004, and there was a statistically significant difference found between groups with respect to distortion.



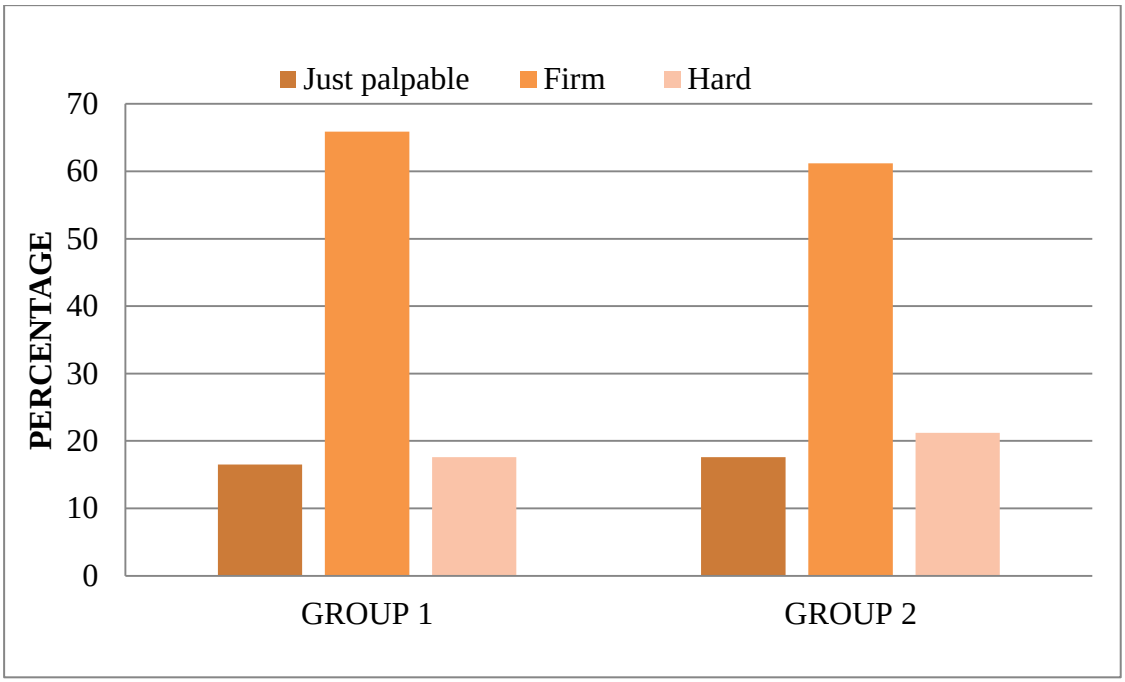
GRAPH 14b: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO DISTORTION AFTER TREATMENT BETWEEN GROUPS

TEXTURE BEFORE TREATMENT	GROUP		TOTAL
	1	2	
Just palpable	14	15	29
	16.5%	17.6%	17.1%
Firm	56	52	108
	65.9%	61.2%	63.5%
Hard	15	18	33
	17.6%	21.2%	19.4%

TABLE 22- DISTRIBUTION OF SUBJECTS ACCORDING TO TEXTURE BEFORE TREATMENT BETWEEN GROUPS

Majority (63.5%) of patients had firm keloids, followed by 19.4% who had hard keloids and 17.1% patients for whom it was just palpable.

P value was 0.796, and there was no statistically significant difference found between groups with respect to texture.



GRAPH 15a: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO TEXTURE BEFORE TREATMENT BETWEEN GROUPS

TEXTURE AFTER TREATMENT	GROUP		TOTAL
	1	2	
Normal	23	10	30
	27%	11.8%	17.6%
Just palpable	48	57	108
	56.5%	67.1%	63.5%
Firm	14	18	32
	16.5%	21.2%	18.8%

TABLE 23- DISTRIBUTION OF SUBJECTS ACCORDING TO TEXTURE AFTER TREATMENT BETWEEN GROUPS

After treatment, majority (63.5%) of patients had just palpable keloids; followed by 18.8% patients who had firm keloid. 17.6% patients even achieved normal texture of the keloid post treatment.

P value was 0.040, there was a statistically significant difference found between groups with respect to texture.

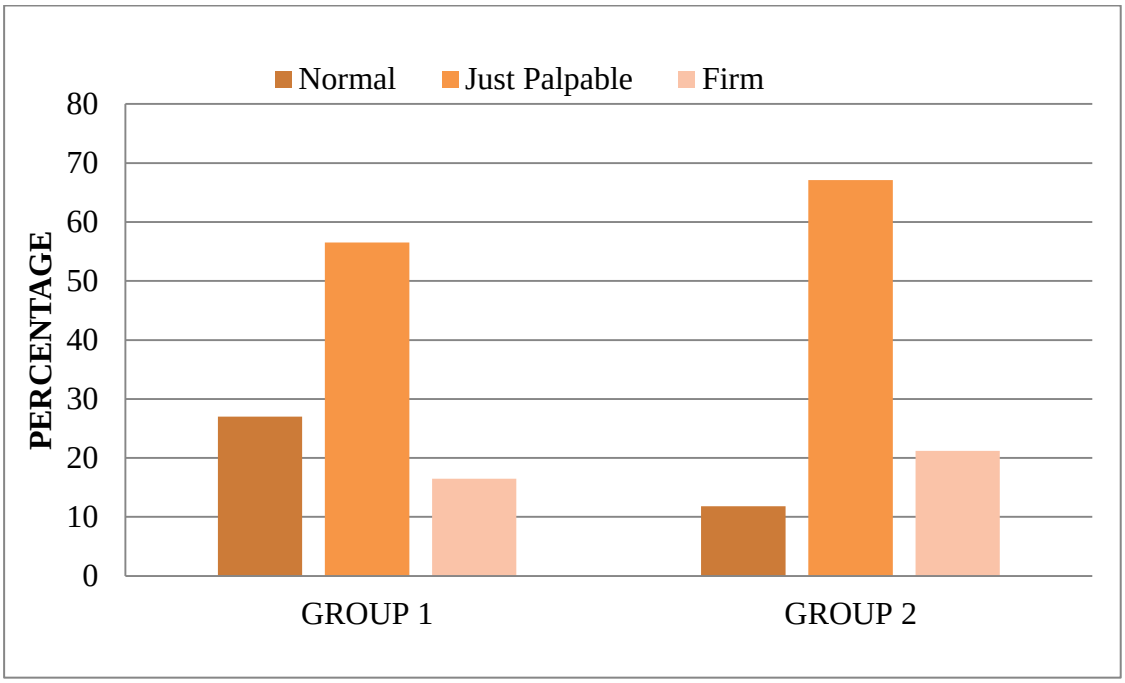
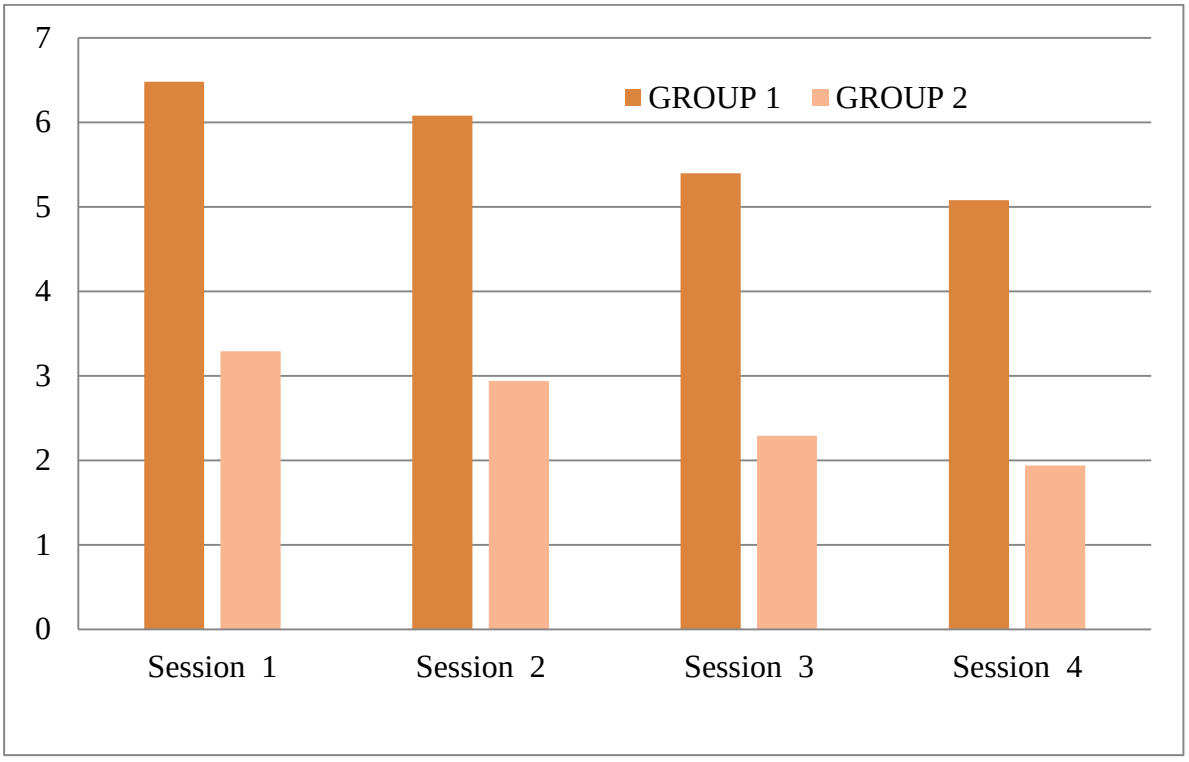


FIGURE 15b: - GRAPH SHOWING DISTRIBUTION OF SUBJECTS ACCORDING TO TEXTURE AFTER TREATMENT BETWEEN GROUPS

PAIN SCORE	GROUP	MEAN	SD	P VALUE
Session 1	**1**	6.48	.995	<0.001
	2	3.29	.814	
Session 2	**1**	6.08	.862	<0.001
	2	2.94	.661	
Session 3	**1**	5.48	.995	<0.001
	2	2.29	.814	
Session 4	**1**	5.08	.862	<0.001
	2	1.94	.661	

TABLE 24: - COMPARISON OF PAIN ON VARIOUS SESSION BETWEEN GROUPS

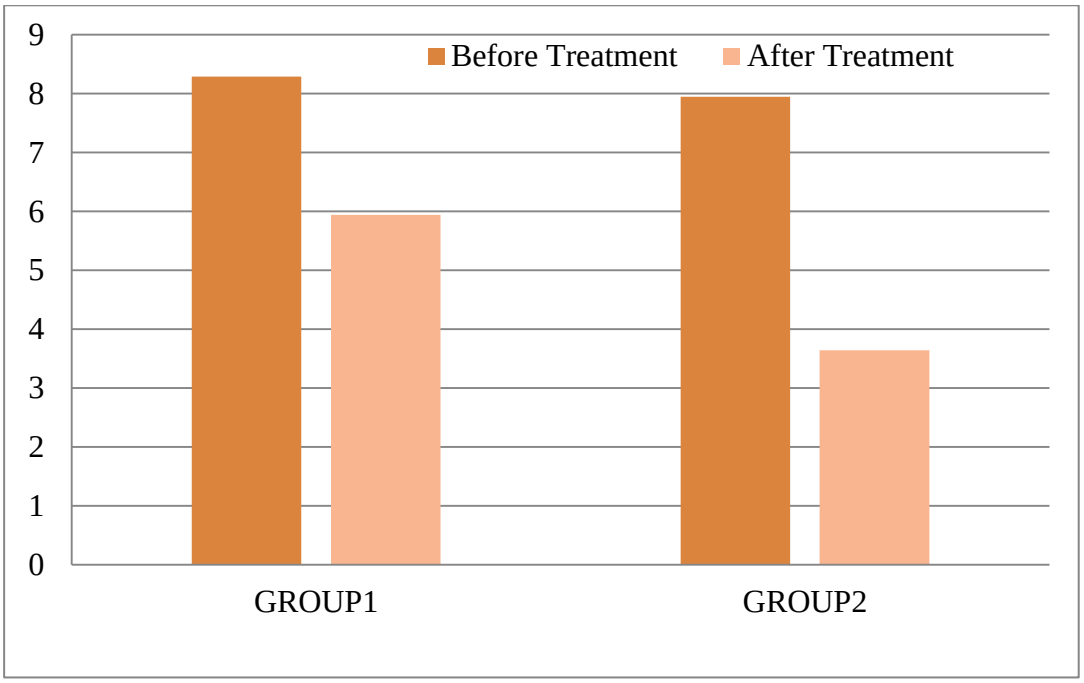
In our study, we found that patients in group 1 experienced more pain than patients in group 2. There was a statistically significant difference found between groups with respect to pain during the treatment.



GRAPH 16: - GRAPH SHOWING COMPARISON OF PAIN ON VARIOUS SESSION BETWEEN GROUPS

VAS SCORE	GROUP	MEAN	SD	P VALUE
Before Treatment	**1**	8.29	.614	<0.001
	2	7.95	.738	
After Treatment	**1**	5.94	.761	<0.001
	2	3.61	.619	

TABLE 25: - COMPARISON OF VAS BETWEEN GROUPS



GRAPH 17: - GRAPH SHOWING COMPARISON OF VAS BETWEEN GROUPS

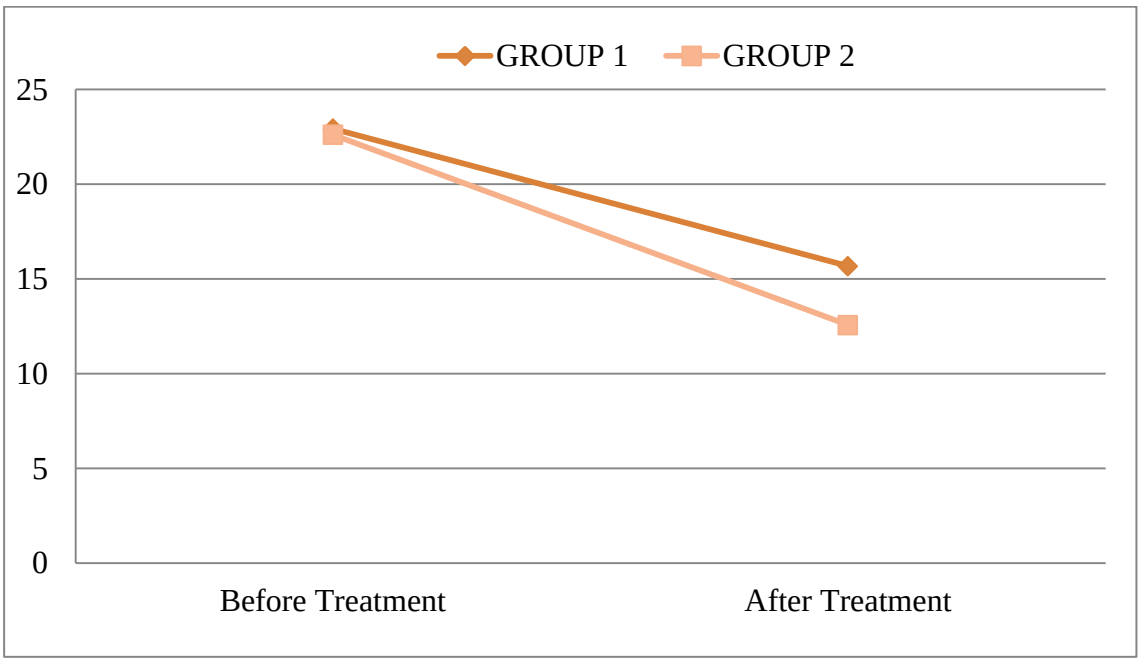
MSS SCORE	GROUP	MEAN	SD	P VALUE
Before Treatment MSS score	**1**	22.92	1.187	0.097
	2	22.60	1.293	
After Treatment MSS Score	**1**	15.67	1.546	<0.001
	2	12.56	1.459	

TABLE 26: - COMPARISON OF MSS SCORE BETWEEN GROUPS

Mean MSS score of patients in group 1 before treatment was 22.92 whereas for patients in group 2 was 22.60.

Mean MSS score of patients in group 1 after treatment was 15.67 whereas for patients in group 2 was 12.56.

There was a statistically significant difference found between groups with respect MSS score after treatment.



GRAPH 18: - GRAPH SHOWING COMPARISON OF MSS SCORE BETWEEN GROUPS

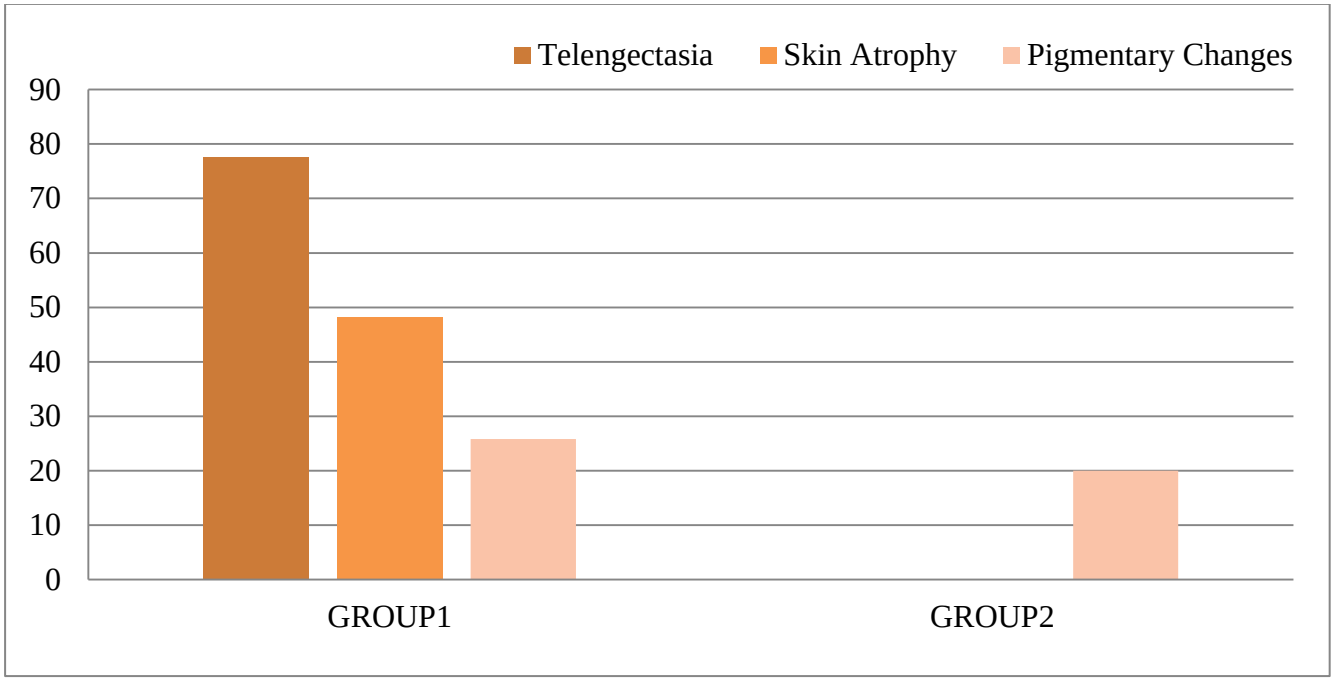
SIDE EFFECTS	GROUP 1	GROUP 2
Telangiectasia	66(77.64%)	0
Skin Atrophy	40(48.2%)	0
Pigmentary Changes	22(25.8%)	17(20%)

TABLE 27: - COMPARISON OF SIDE EFFECTS BETWEEN GROUPS

The most common side effect seen in patients after treatment was telangiectasia, seen exclusively in patients in Group 1, followed by skin atrophy, which was seen in 48.2% of the patients of Group 1.

Patients in both the groups had pigmentary changes, hypo or hyperpigmentation, with 25.8% from group 1 and 20% from group 2.

P value was 0.001, there was a statistically significant difference found between groups with respect to side effects post-treatment.



GRAPH 19: - GRAPH SHOWING COMPARISON OF SIDE EFFECTS BETWEEN BOTH GROUPS AFTER TREATMENT

DISCUSSION

DISCUSSION

AGE WISE DISTRIBUTION

In this study, majority (31.8%) of the patients belonged to the age group of 31- 40 years, followed by 25.3% of patients in the age group of 21-30 years. The total range of age was from 12-60 years. More than 50% of the patients were within the age of 40 years.

In studies conducted by Berman et al[1] and Murray[121], the onset of keloids was reported most commonly between 10 and 30 years of age and uncommon at age extremes.

Cosman and associates[5] observed that most patients presented for their initial treatment at an average age of 22.8 years and the median age of onset was 22.3 years in women and 22.6 years in men.

Ketchum et al[37] also found that keloids occur in the younger age groups. Around 88% of lesions occurred in patients less than 30 years of age. The possible explanation for this finding is that youngsters are more frequently subjected to trauma. Skin tension and rate of collagen synthesis is also higher in younger individuals.

The findings in the present study are hence in concordance with those of the above mentioned studies.

The difference in age distribution between the two regimens was found to be non-significant ($p>0.05$).

SEX WISE DISTRIBUTION

Out of 170 patients, 53.5% were males and 46.5% were females with a male to female ratio of 1.15:1.

This is in accordance with the study conducted by Ketchman et al[37], who also reported an almost equal incidence among both the sexes.

In the study including 65 patients, Darzi et al[122] found 61.5% were females and 38.5% were males, possibly reflecting the greater cosmetic concern about keloids and increased incidence of ear piercing in females. Udo-Affah et al[119] also reported a slightly higher incidence in females (51.2%) than males (48.8%).

In the present study, the slightly higher male preponderance could either signify an increasing cosmetic concern or reduced compliance to monotherapy among males.

OCCUPATION

Of the 170 patients recruited for the study, majority (49.4%) were unskilled workers followed by 34.1% semi-skilled workers 16.5%) being skilled workers. This observation may be attributed to cosmetic defect, distressing symptoms and non-compliance to monotherapy, among this population.

FAMILY HISTORY

In the present study, 4.7% of patients had a positive family history, Berman et al[1] reported a familial incidence ranging from 4% to 16% in black and Hispanic population. Bayat et al[125], in their study reported a familial incidence of 50%.

In familial cases, the exact mode of inheritance is unclear and both autosomal recessive and autosomal dominant patterns of inheritance have been reported.[29,12]

NUMBER OF LESIONS

In this study, majority (85.9%) of patients presented with only one keloid, while 14.1% of patients presented with multiple (2 or more) keloids. It was observed that multiple lesions developed either spontaneously or following multiple skin injury such as acne, folliculitis or chicken pox.

SITE OF LESION

In this study, keloids were most commonly found on the mid-sternum (36.45%), followed by shoulder (24.1%), earlobe (22.9%), upper extremity (15.3%) and lower extremity (6.2%). 11.1% patients had keloids on other parts of the body.

While keloids may be found anywhere on the body, they have a predilection for certain sites such as chest, shoulders, back, upper limbs and ears.[5]

According to a study by Berman et al[1], the most frequently involved sites were chest, shoulders, head and neck areas (mainly the earlobes), arms and upper back.

Muir et al[123], also found a higher incidence of keloids over the presternal area followed by deltoid and ear. Bayat et al[124] also observed that keloids occur most commonly over the chest, shoulder, upper back, nape of neck and ear lobes.

The results of the present study are in agreement with those of the above mentioned studies.

SIZE OF THE KELOID

Majority of the patients had keloid measuring <2 cm in the largest diameter, followed by 18.2% patients who had keloids measuring between 2-5 cm and 18.2% patients for whom the keloids measured >5cm.

PRESENTING SYMPTOMS AND SIGNS

Out of 170 patients, 70.6% of patients presented with cosmetic disfigurement and 25.9% complained of pruritus, which were of mild or moderate intensity. 3.5% of the patients came seeking for medical intervention for job purposes.

In the study by Berman et al[1], pruritus, pain, cosmetic disfigurement, skin discoloration and restriction of movements were the presenting complaints.

The main presenting symptoms in the study by Nanda et al[126] were itching (64.3%), pain (21.4%), cosmetic reasons (21.4%) and restriction of movement (7.1%).

According to Kelly[5], cosmetic concern is the main reason for which patients seek medical intervention.

The observations in the present study are in concordance with the aforesaid mentioned studies. Of the patients complaining of pruritus, 79.5% had improvement (reduction) in pruritus after treatment. In a study by Griffith et al[91], of the 37 patients treated with only triamcinolone acetonide injection, there was relief of symptoms in all cases. Berman et al[1] also observed significant response rates ranging from 50-100% using triamcinolone acetonide alone. The results in our study are in concordance with these study.

Keloids are characterized as more clinically severe in nature, causing pruritus and pain more frequently in patients.[34]

Studies have shown that when the keloid is growing, it can feel itchy, painful, or both. Most often, keloids on the chest are tender as compared to keloids over other areas. Once a keloid stops growing, symptoms usually stop.[36] Most cases in our study presented with pruritus, but complaints of pain wasn't noted in any.

Some studies have also shown that the keloids become darker in color with time, once a keloid stops growing. The border is usually darker than the center.[36] However any such finding was not seen in patients in our study.

RESPONSE OF PATIENTS TO RESPECTIVE REGIMENS

In this study, the primary outcome evaluated based on the Manchester Scar Scale scoring and it was considered as the main parameter of efficacy. Patients in both the regimens were comparable with respect to age, sex, site and number of lesions, with statistically no significant difference ($p>0.05$).

Observation of keloids prior-to and post-treatment, based on individual parameters of MSS as follows-

I. Color

Regimen I: Cryotherapy with intralesional triamcinolone acetonide injection

55.3% of patients came with obvious mismatch of color of keloid with the surrounding skin, followed by 30.6% patients who had slight mismatch. 14.1% of patients however had gross mismatch of color with the surrounding skin. Following treatment, majority (65.9%) of patients just had slight mismatch of color with the surrounding skin. However, 34.1% patients continued to have obvious mismatch of color. There was no patient who had perfect color match of the treated keloid with the surrounding skin.

Regimen II: Fractional CO2 LASER with Topical Betamethasone

Prior to treatment, 54.1% of patients had obvious mismatch of color of keloid with the surrounding skin, followed by 35.3% patients who had slight mismatch. 10.6% of patients had gross mismatch of color with the surrounding skin. It was encouraging to see 16.55 patients having perfect match ok keloid color with the surrounding skin, providing treatment satisfaction to the patient. 80% of patients just had slight mismatch of color, while a meager 3.5% of patients continued to have obvious mismatch of color with the surrounding skin after treatment.

P value – Not statistically significant difference before treatment; however it was <0.001, showing a statistically significant difference between both regimens after treatment.

In this study, we found that dyschromia showed more improvement as a result of topical steroid plus laser therapy, which is in line with the findings of Behrangi et al.[127] Also Waibel

et al. demonstrated good response of texture in patients under treatment with laser plus triamcinolone, but in their study, dyschromia did not show good response to this treatment probably because their study had no comparison group. [128]

II. Finish

Regimen I : Cryotherapy with intralesional triamcinolone acetonide injection

All subjects had a shiny finish of the keloid. Post treatment, none of the patient in group 1 had any improvement in the finish of the keloid even after receiving the treatment.

Regimen II : Fractional CO2 LASER with Topical Betamethasone

Prior to treatment, all subjects had a shiny finish of the keloid. 47.1% (40) of subjects had improvement in the finish of the keloid. The keloid surface lost its shine and had a matte finish of the surface, making it more aesthetically acceptable for the patients.

P value - <0.001, which was statistically significant between both groups with respect to finish of the keloid.

III. Contour

In both the groups, the contour before treatment was keloid in all the subjects.

Regimen I : Cryotherapy with intralesional triamcinolone acetonide injection

Post treatment – 64.7% patients had slightly raised or indented contour followed by 27.1% patients for whom the keloid had flushed with the surrounding skin. However 8.2% patients continued to have hypertrophic contour without much improvement, even after 4 treatment sessions.

This is in concordance with another study where it took around 20 sessions to achieve totally acceptable results.[26]

Regimen II : Fractional CO2 LASER with Topical Betamethasone

Post treatment – Larger proportion (44.7% vs 27.1%) of subjects had achieved "flushed with surrounding skin" contour as compared to patients in Group 1. 52.9% patients continued to have a slightly raised of indented contour. A negligible proportion (2.4%) of patients had hypertrophic contour .

P value - 0.023, which was statistically significant between groups with respect to contour.

A study by Alexander et al, showed more than 50% improvement in the degree of hypertrophy of the 40% of the lesions treated in the study.[129]

IV. <u>Distortion</u>

Regimen I : Cryotherapy with intralesional triamcinolone acetonide injection

70.6% of the patients had moderate distortion, followed by 25.9% of the patients who had mild distortion prior to treatment. After 4 treatment sessions, 71.6% of patients had mild distortion while 25.9% had none.

Regimen II : Fractional CO2 LASER with Topical Betamethasone

A huge proportion (60%) of patients had moderate distortion while 26.55 of patients had mild distortion of the keloid, prior to treatment. Post treatment, comparable proportion (72.9%) of patients had mild distortion and 12.9% had none.

P value – 0.004, showed statistically significant difference between both groups with respect to distortion with Regimen I showing better improvement than Regimen II.

The results in our study are similar to the results of a study conducted by Beharangi, where the general appearance of the wound was better in the intralesional triamcinolone acetonide injection treated lesions.[127]

V. Texture

Regimen I : Cryotherapy with intralesional triamcinolone acetonide injection

65.9% of patients had firm keloid, 17.5% had hard while 16.5% had just palpable texture prior to treatment. Post treatment,27% had attained normal texture, 56.5% had just palpable whereas 16.5% had firm texture of the keloid.

Regimen II : Fractional CO2 LASER with Topical Betamethasone

Majority (61.2%) patients had firm keloid, followed by 19.4% who had hard texture prior to treatment. 67.1% had just palpable texture while 17.6% had achieved a normal texture by the end of the treatment.

P value - 0.040, which was statistically significant between both groups with respect to texture.

This result is in concordance to a study conducted by Beharangi where the group receiving Fractional CO2 Laser with topical steroids had better improvement in texture.[127] Waibel et al. in his study also demonstrated good response of texture in patients under treatment with laser plus triamcinolone.[128]

Overall improvement in keloid after treatment as per the MSS score indicates that greater the magnitude of the decrease, the greater the improvement of the keloid.

Regimen I : Cryotherapy with intralesional triamcinolone acetonide injection

Of the 85 patients, the mean MSS score before treatment was 22.92 and standard deviation 1.187. After treatment, the MSS score reduced to 15.67 with standard deviation 1.546. There was mean reduction of 31.6% of MSS score post treatment.

Studies have shown that contact spray cryotherapy with intralesional triamcinolone acetonide injection can bring about 68-81% remission with <2% recurrence. But around 20 sessions are required to achieve these results.[26]

A study by Har-Shai et al[26], reported an average of 51.4% reduction in scar volume following just one session of cryotherapy.

A systematic review of eight studies by Van Leeuwen et al[130], reported that the decrease in average scar volume ranged from 51-63% following intralesional cryotherapy.

Another recent study by Tziotzios et al[131], showed scar volume reductions of 70% for ear keloids and 60% for keloids on the upper back, shoulder and chest were achieved following single cryosessions.

The better response seen in the present study could be attributed to the additional intralesional injection of triamcinolone acetonide after each cryotherapy session.

In regimen II : Fractional CO2 LASER with Topical Betamethasone

Of the 85 patients, the mean MSS score before treatment was 22.60 and standard deviation 1.293. After treatment, the MSS score reduced to 12.56 with standard deviation 1.459. There was mean reduction of 44.4% of MSS score post treatment.

Another recent study by Behrangi et al, concluded that local corticosteroids plus fractional laser therapy was more effective than intralesional corticosteroids injections for the improvement of dyschromia and texture of hypertrophic and keloid scars.[127]

Alster reported that intralesional corticosteroid injection plus laser had no additional effects over treatment with PDL alone, which is not in congruence with our results.[132]

PAIN ASSESSMENT

In our study, we found that patients in group 1 experienced considerably more pain than patients in group 2. There was a statistically significant difference found between groups with respect to pain experienced during the treatment.

In the study of Teplyi V et, pain and itching were reduced in 73.3% with triamcinolone betamethasone.[133] In this study, reduction in pain was statistically significant in both the groups.

The high pain associated with Regimen I might be a reason for high dropout rates seen in patients on cryotherapy with intralesional triamcinolone.

TREATMENT OUTCOMES IN BOTH THE REGIMENS

Among the two regimens, both regimens had good response. However, the treatment outcome between the two regimens was statistically significant, ($p<0.05$) with regimen II showing faster and more cosmetically acceptable results at the end of 4 treatment sessions.

SIDE EFFECTS

The side effects of both the regimens were also studied to assess the safety of the regimens.

The most common adverse effects were seen 1-2 months after starting the treatment sessions.

Of the 170 patients included in the study, 60% of patients developed complications, of which majority (83.3%) of patients belonged to regimen I and rest (16.7%) of the patients belonged to regimen II.

In regimen I, of those who developed complications, pain was one parameter which

reduced after 5-6 hours after treatment.

However, most adverse effects like telangiectasia (77.64%), atrophy (48.2%) and pigmentary changes (25.8%) persisted.

Goldenberg et al[17] reported hypopigmentation, local edema and epidermolysis as the observed side effects following intralesional cryotherapy.

Gupta and Kumar[26], in their study, also reported hypopigmentation / depigmentation along the needle tracks in all cases, which improved during the follow-up period.

In regimen II, 17% of the cases developed pigmentary changes (hypo/hyperpigmentation).

The commonest side effects observed with intralesional steroid are skin atrophy, hypo/hyper pigmentation and development of telangiectasias[134]. Systemic side effects like Cushing's syndrome have also been reported by few.[96]

The results in our study are consistent with results of another study by Behera et al and Emad et al, where there was reduced the incidence of hypopigmentation and atrophy in group receiving Fractional CO2 Laser treatment.[135-137]

In a study by Alexander et al, Fractional CO2 + ILS group had more side effects compared to ILS only group, though the difference was not statistically significant.[129]

In the present study, Group II had remarkably lesser side effects resulting in better acceptability and compliance with the treatment.

CONCLUSION

CONCLUSION

- More than 50% of the patients were within the age of 40 years. This could be because people in this age group are more prone to trauma and show increased frequency of ear piercing.
- The gender wise distribution was almost equal with a slight male preponderance due to the growing cosmetic concern and reduced compliance to monotherapy among males.
- Almost half of the total cases were unskilled workers like home-makers, farmers, manual labourers, etc or students owing to the fact that patients are more concerned about the cosmetic blemish, while farmers are more concerned about symptoms like pruritus and they also have a tendency to be less compliant to monotherapy.
- Overall, chest/mid-sternum was the commonest site involved, which is also the established region for occurrence of keloid.
- Infection or trauma over a single site, constituted majority of the provoking factor for the development of single keloid in majority of patients.
- A very small proportion of patients gave a positive family history of keloids.
- Cosmetic disfigurement and itching were considered the presenting complaints in majority of the patients, which happens to be the most common symptoms in patients with keloids.
- Both the regimens were found to be efficacious, showing the effect of combination therapy in the management of keloids. However, regimen II achieved excellent response when compared to regimen I.
- Majority of the patients showed excellent response irrespective of the duration and site of lesions signifying that both regimens can be used to effectively treat all lesions

of any duration, occurring at any site.

- Side effects were considerably more in regimen I than regimen II. Most of these side effects were persistent and irreversible, making them cosmetically unacceptable.

Finally, based on the above observations, the following conclusions can be drawn:-

1. Combination therapies are highly effective in treatment of keloids, especially those resistant to standard monotherapies.
2. Of the two regimens, although both combinations were equally efficacious, rate of improvement was better with regimen II.
3. However, based on the side effect profile, wherein more troublesome and persistent complications were observed in regimen I, regimen II was considered to be far safer and with aesthetically superior outcomes.

SUMMARY

SUMMARY

One seventy patients were included in this study, divided into two groups of 40 each to receive two different regimens.

- Around half of the patients belonged to the 4th decade of life.
- There was a slight female preponderance.
- Housewives, farmers, labourers and workers constituted almost half of the total cases.
- Chest was the most common site (36.45%) involved followed by shoulder (24.1%) and earlobe (22.9%).
- About 4/5th of patients presented with a single keloid.
- Family history of keloids was positive in about 5% of cases.
- Cosmetic disfigurement was the commonest presenting symptom seen in 70.6% of patients followed by pruritus in 25.9%, which were of mild or moderate intensity.
- In regimen I (Cryotherapy with intralesional triamcinolone acetonide injection), the mean MSS score reduced by 31.6% after treatment (22.92 to 15.67).
- In regimen II (Fractional CO2 LASER with topical betamethasone), mean MSS score reduced by 44.4% post treatment (22.60 to 12.56).
- Overall, side effect were seen in only 60% of cases of which majority (83.3%) of patients belonged to regimen I. The immediate side effects in regimen II like crusting were more significant than those in regimen I.

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BIBLIOGRAPHY

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ANNEXURE

ANNEXURE I

PROFORMA

Name: **Age:** **Sex:** M/F

OP No.: **Education:**

Address: **Occupation:**

Ph No.:

Email id:

C/C:-

HOPI:-

Drug history:-

Past history:- DM/ HTN/ TB/ Epilepsy/ Asthma/ Atopy.

Others -

Family history:- DM/ HTN/ TB/ Epilepsy/ Asthma/ Atopy.

Others -

Personal history:-

Diet – veg/ non-veg/ mixed Appetite –

Sleep – adequate/ disturbed Bowel & Bladder –

Other habits –

Menstrual/Obstetric history:-

Surgical history:-

Occupational history:-

General physical examination:-

PR = bpm BP = / mmHg

RR = cpm Temperature =

P I C C L E Others –

Systemic examination:-

CVS – RS –

P/A – CNS –

Local examination:-

Skin –

Fitzpatrick skin type:

Hair –

Oral mucosa –

Nails –

Keloids:-

I. Size of keloid-

II. Site of keloid –

III. Contour –

- perfect
- slight mismatch
- obvious mismatch
- gross mismatch

IV. Finish –
    - Matte
    - Shiny

V. Contour –

- flushed with surrounding skin
- slightly raise or indented
- hypertrophic
- keloid

VI. Distortion-

- none
- mild
- moderate
- severe

VII. Texture

- normal
- just palpable
- firm
- hard

VAS Score :

Investigations:-

CBC:

Hb%= mg/dl ESR= mm/hr AEC= cells/mm^3

RBC= M/mm^3 WBC= T/mm^3 Plt= L/mm^3

RBS= mg/dl HbA1c =

BT= CT= APTT=

LFT= RFT=

ICTC= HbSAg=

Diagnosis:-

Treatment:-

ANNEXURE II

CONSENT FORM

"A COMPARATIVE STUDY OF EFFECTIVENESS OF CRYOTHERAPY WITH INTRALESIONAL TRIAMCINOLONE VS FRACTIONAL CO2 LASER WITH TOPICAL BETAMETHASONE FOR THE TREATMENT OF KELOIDS.**"**

I, Mr./Mrs./Ms. _____, aged _____ years, S/D/o _____, & a resident of _____ _____ _____, do hereby declare that I am voluntarily giving my consent to participate/ let my son/ daughter to participate in the study of "A COMPARATIVE STUDY OF EFFECTIVENESS OF CRYOTHERAPY WITH INTRALESIONAL TRIAMCINOLONE VS FRACTIONAL CO2 LASER WITH TOPICAL BETAMETHASONE FOR THE TREATMENT OF KELOIDS.".

I have been explained in my own language about the nature of my skin condition, its prognosis, the treatment options available & their respective side effects. I have also been explained to my full satisfaction, in my own language about the procedure involved in the study. I have been explained that my refusal to consent is however not going to affect my / my patient's right to receive treatment from the department.

I do hereby declare that I will provide complete medical history of the disease, allow myself/ my patient to undergo clinical examination & allow collection of necessary clinical material by the treating Doctor.

I also hereby accord consent to be photographed as & when necessary for the purpose of the study. However, these photographs have to be used only for teaching purposes, clinical presentations & publications but not for advertisements or any other commercial purposes.

Name of the declarant / guardian _____

Signature of the declarant / guardian _____

Name of the witness: _____

Signature of the witness: _____

Name & Signature of the investigator: _____

Date: _____ Place: SDUAHER, KOLAR.

ANNEXURE III

PATIENT INFORMATION SHEET

Study Title: A COMPARATIVE STUDY OF EFFECTIVENESS OF CRYOTHERAPY WITH INTRALESIONAL TRIAMCINOLONE VS FRACTIONAL CO2 LASER WITH TOPICAL BETAMETHASONE FOR THE TREATMENT OF KELOIDS

Study Site: R.L Jalappa Hospital ,Tamaka, Kolar.

Aim:1) To compare the therapeutic effectiveness of Cryotherapy with Intralesional Corticosteroid and Fractional CO2 laser followed by topical corticosteroids in the treatment of keloids

2) To assess the efficacy of Fractional CO2 laser with topical steroid in the treatment of keloids

3) To assess the efficacy of cryotherapy with intralesional corticosteroid in the treatment of keloids

Keloids and hypertrophic scars are abnormal responses of body to skin injuries. Overproduction of compacted fibrous tissue is the basic cause of these lesions. Intralesional corticosteroids form the first line of treatment of keloids. Many different treatment modalities have been implicated in their management, but currently there is no entirely satisfactory method for treating all keloid lesions.

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in this study, we will collect information(as per proforma) from you. Relevant blood investigations will be carried out if required. This information collected will be used for dissertation and publication only.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. The expenses required for the above

investigations will be funded by the study investigator. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For any further clarification you can contact the study investigator:

Dr. Nishi Nagaria

Mobile no: 9901302312

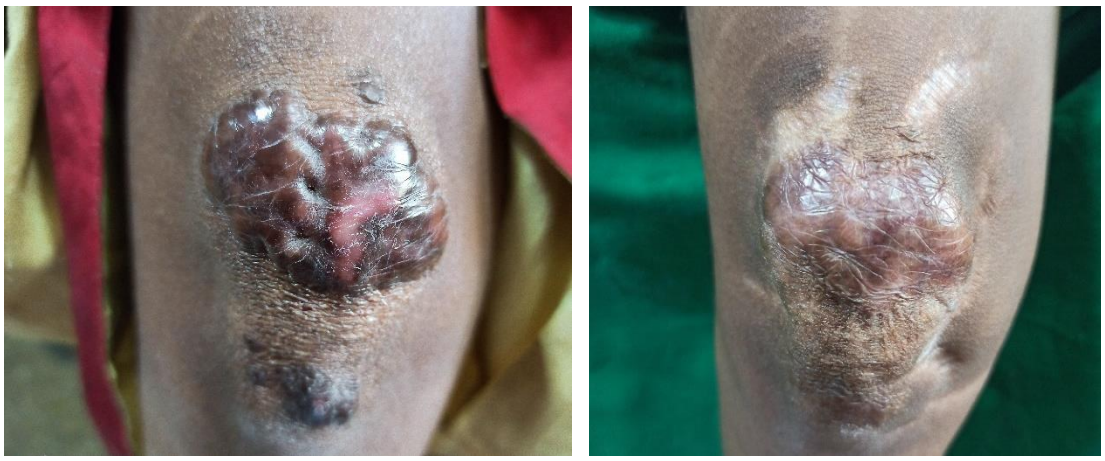
E-mail id: nishinagaria@yahoo.com

ANNEXURE IV

GROUP 1

(CRYOTHERAPY WITH INTRALESIONAL TRIAMCINOLONE ACETONIDE INJECTION)

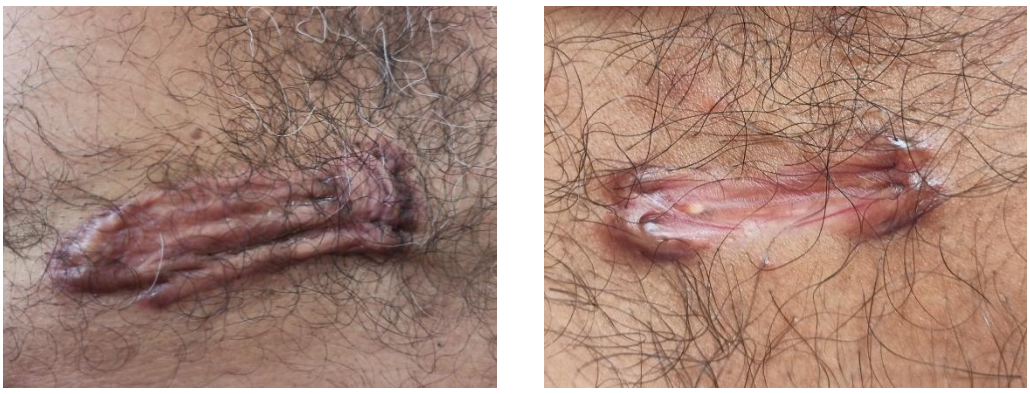
Patient 1



Pre-Treatment **Post-Treatment**

Photograph 3

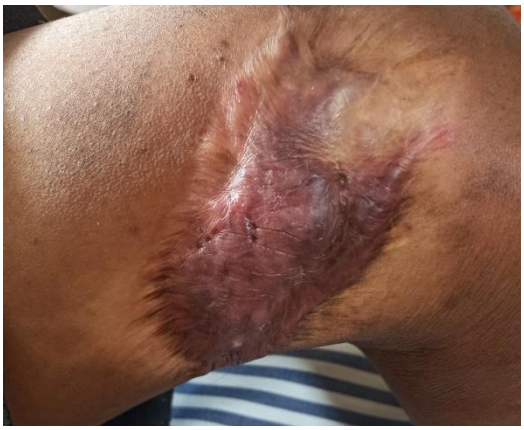
Patient 2

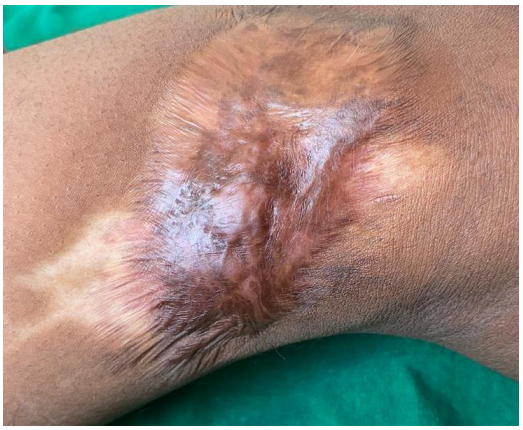


Pre-Treatment **Post-Treatment**

Photograph 4

Patient 3





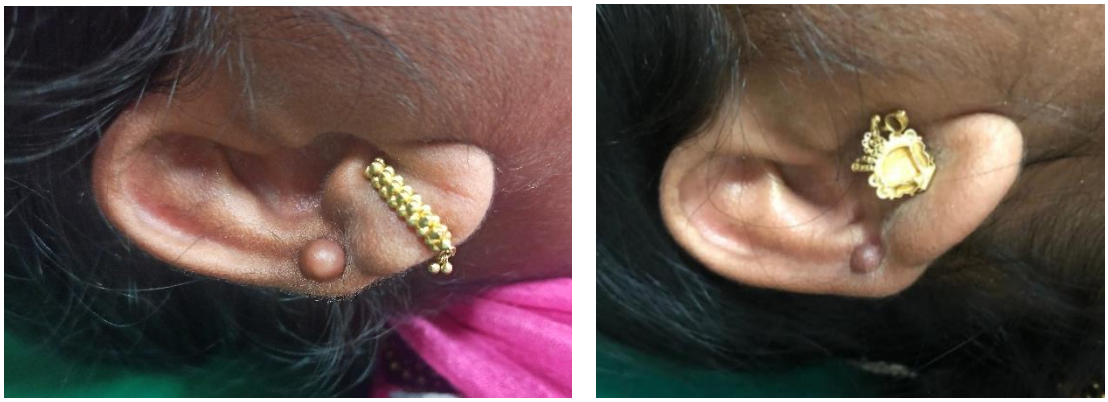
Pre-Treatment **Post-Treatment**

Photograph 5

GROUP 2

(FRACTIONAL CO2 LASER WITH TOPICAL BETAMETHASONE)

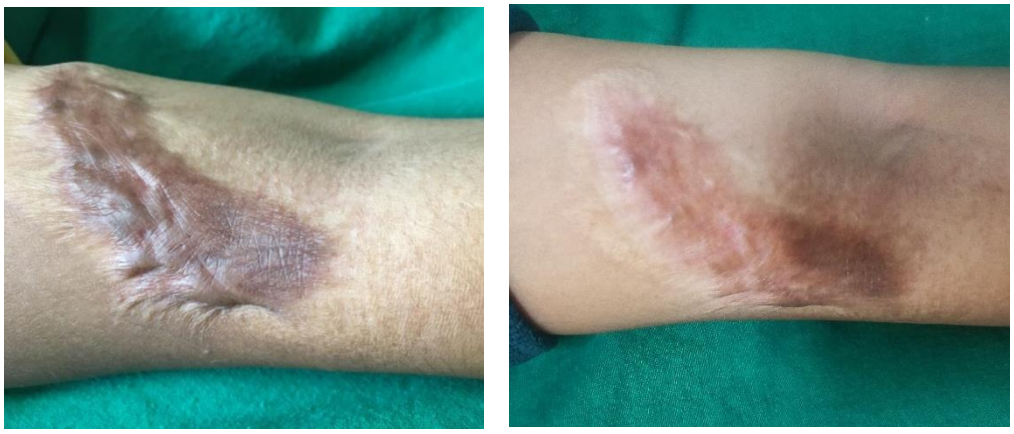
Patient 1



Pre-Treatment **Post-Treatment**

Photograph 6

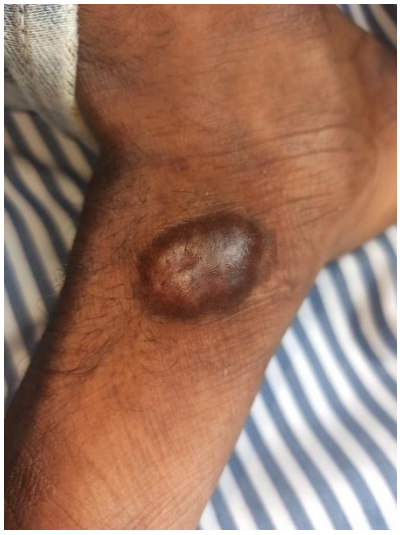
Patient 2

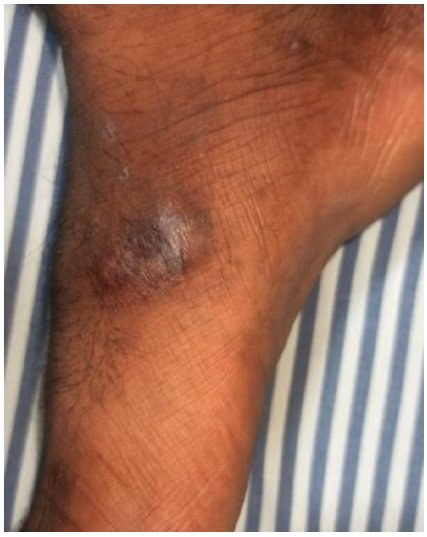


Pre-Treatment **Post-Treatment**

Photograph 7

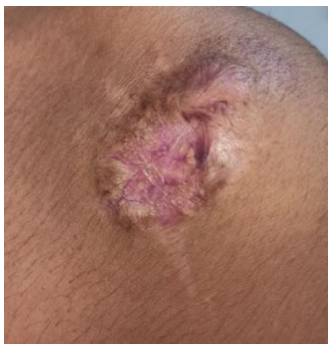
Patient 3



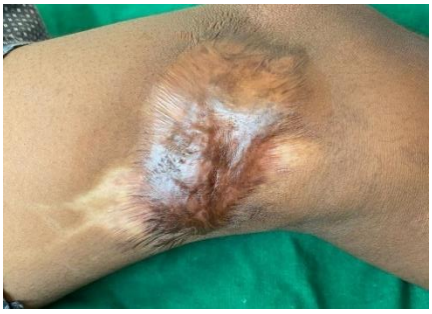


Pre-Treatment **Post-Treatment**

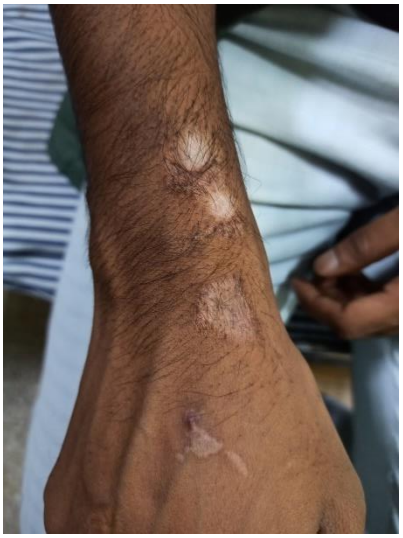
Photograph 8



Photograph 9 - Side effects – Telangiectasia and Atrophy



Photograph 10 - Side effects – Atrophy due to lymphatic uptake of Triamcinolone Acetonide



Photograph 11 - Side effects – Atrophy and Hypopigmentation

ANNEXURE V

KEY TO MASTER CHART

Size Of Keloids:

1. <2cm
2. 2-5cm
3. >5cm

Site Of Lesion:

1. Mid Sternum
2. Ear Lobe
3. Arm
4. Shoulder
5. Legs
6. Others

Side Effects:

1. Telangiectasia
2. Skin Atrophy
3. Pigmentary Changes (Hypo/Hyperpigmentation)
4. Skin Necrosis
5. Ulceration

MASTER CHART

ILS Triamcinolone with Cryotherapy																														
Sl. No	UHID	Age	Sex	Occupation	Family History	Number of Keloids	Site of the Keloid	Size of keloid	Pruritus	Improvement in pruritus after treatment	Reason for Treatment	Pain during treatment				Colour		Finish		Contour		Distortion		Texture		Visual Analogue Scale		MSS Score		Side Effects	Hypo/Hyperpigmentation
												Session 1	Session 2	Session 3	Session 4	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment		
1	672904	39	M	farmer	no	multiple	1,3,4	3	yes	yes	symptomatic relief	7	6	6	5	4	3	2	2	4	1	3	2	3	2	8	6	24	16	2	
2	601671	30	M	accountant	no	single	3	3	no		cosmetic relief	8	7	7	6	3	2	2	2	4	1	3	2	4	3	9	7	25	17	1	
3	672701	31	M	dailywedge worker	no	single	2	2	yes	yes	symptomatic relief	7	7	6	6	2	3	2	2	4	3	3	2	4	3	8	6	23	19	1,2	
4	648920	36	F	home maker	no	multiple	1,2,3	3	no		cosmetic relief	8	7	7	6	3	2	2	2	4	1	3	2	4	3	9	7	25	17	2	
5	838944	46	M	factory worker	no	multiple	4,6	3	yes	yes	symptomatic relief	9	8	8	7	3	3	2	2	4	2	3	2	3	3	8	6	23	18	1	
6	850349	17	M	student	yes	single	2	1	no		cosmetic relief	7	6	6	5	2	2	2	2	4	1	4	3	4	3	9	7	25	18	1,2	
7	853649	46	F	home maker	no	single	3	1	no		cosmetic relief	6	6	5	5	3	3	2	2	4	2	3	2	3	2	9	7	24	18	1	
8	737014	35	M	construction worker	no	single	4	2	yes	yes	symptomatic relief	7	6	6	5	2	2	2	2	4	2	2	1	3	2	8	6	21	15	1,2,3	hypopigmentation
9	859717	45	M	factory worker	no	multiple	3,4,6	2	no		job purpose	5	5	4	4	3	3	2	2	4	1	2	1	3	2	9	7	23	16	1	
10	859855	46	F	home maker	no	multiple	1,2,5	3	yes	no	symptomatic relief	6	6	5	5	4	2	2	2	4	1	3	2	3	2	8	6	24	15	2	
11	859855	45	M	bank manager	no	single	4	3	yes	yes	symptomatic relief	7	6	6	5	3	3	2	2	4	3	2	2	4	3	9	7	24	20	1	
12	866430	20	M	student	no	single	3	2	no		cosmetic relief	8	7	7	6	2	3	2	2	4	1	2	2	4	3	8	6	22	17	1,2	
13	893014	45	M	dailywage worker	yes	single	1	1	yes	no	symptomatic relief	7	7	6	6	3	2	2	2	4	2	3	2	3	2	8	7	23	17	1	
14	893104	13	F	student	no	single	3	1	no		cosmetic relief	6	6	5	5	4	3	2	2	4	1	2	1	3	2	8	7	23	16	2	
15	587914	55	M	factory worker	no	single	3	1	no		cosmetic relief	7	7	6	6	3	3	2	2	4	1	3	2	3	3	9	6	24	17	1,2	
16	565176	46	M	accountant	no	single	6	3	yes	yes	symptomatic relief	8	7	7	6	2	2	2	2	4	2	2	1	3	2	9	7	22	16	1	
17	537265	32	F	home maker	no	single	2	3	no		cosmetic relief	7	7	6	6	3	3	2	2	4	2	3	2	3	2	8	6	23	17	2	
18	624079	47	M	truck driver	no	single	1	1	no		cosmetic relief	6	6	5	5	2	3	2	2	4	2	3	1	4	3	9	6	24	17	3	hypopigmentation
19	537320	31	F	bank manager	no	single	1	1	no		cosmetic relief	5	5	4	4	3	2	2	2	4	1	3	1	3	2	8	7	23	15	1,2	
20	609621	41	M	driver	no	multiple	1,2,4	3	no		cosmetic relief	7	7	6	6	2	2	2	2	4	2	3	2	3	2	9	7	23	17	1	
21	661401	48	F	home maker	no	single	5	1	no		cosmetic relief	5	5	4	4	3	3	2	2	4	1	2	1	2	1	8	6	21	14	2	
22	609742	36	F	home maker	no	single	5	2	no		cosmetic relief	8	7	7	6	2	3	2	2	4	2	3	2	3	1	9	7	23	17	1	
23	526870	53	M	teacher	no	single	2	3	yes	no	symptomatic relief	7	7	6	6	3	2	2	2	4	1	3	2	2	2	8	6	22	15	1,3	hypopigmentation
24	607222	42	F	home maker	no	single	6	3	no		cosmetic relief	6	6	5	5	3	2	2	2	4	2	3	2	3	1	9	7	24	16	1,2	
25	593189	36	F	home maker	no	single	1	1	no		cosmetic relief	7	6	6	5	3	2	2	2	4	1	2	1	2	1	8	6	21	13	1	
26	564762	46	F	home maker	no	single	1	1	no		cosmetic relief	6	5	5	4	2	2	2	2	4	2	3	2	3	2	9	7	23	17	2	
27	850020	23	M	student	no	single	2	1	no		cosmetic relief	6	6	5	5	3	2	2	2	4	1	3	2	3	1	8	6	23	14	2	
28	851905	39	M	buisnessman	no	single	1	3	yes	yes	symptomatic relief	5	5	4	4	3	2	2	2	4	1	3	2	3	2	7	5	22	14	1,2	
29	839598	35	F	home maker	no	single	4	1	no		cosmetic relief	6	5	5	4	2	2	2	2	4	2	3	2	4	1	8	6	23	15	1	
30	849262	45	M	farmer	no	single	4	1	yes	yes	symptomatic relief	7	7	6	6	3	2	2	2	4	2	3	2	3	2	9	7	24	17	1	
31	849818	26	F	home maker	no	single	1	1	no		cosmetic relief	7	6	6	5	2	2	2	2	4	3	4	3	4	2	8	6	24	18	1,3	hypopigmentation
32	851896	33	F	home maker	no	single	5	2	no		cosmetic relief	6	6	5	5	3	2	2	2	4	1	3	2	3	2	9	7	24	16	1,2	
33	850026	35	F	home maker	no	single	2	2	no		cosmetic relief	5	5	4	4	2	2	2	2	4	2	2	1	3	2	8	7	21	16	1	
34	834670	48	M	construction worker	no	single	6	1	yes	no	symptomatic relief	7	7	6	6	3	2	2	2	4	2	3	2	3	2	8	6	23	16	1,2	
35	842164	35	M	construction worker	no	single	1	1	no		cosmetic relief	6	6	5	5	2	2	2	2	4	2	3	2	3	2	7	7	21	17	1	
36	846340	42	M	buisnessman	no	single	2	1	no		cosmetic relief	5	5	4	4	4	3	2	2	4	3	3	2	3	2	8	6	24	18	2	
37	851794	24	F	home maker	no	single	1	1	no		cosmetic relief	7	6	6	5	3	3	2	2	4	1	3	2	4	3	8	7	24	18	3	hypopigmentation
38	850476	50	M	construction worker	no	single	2	1	yes	yes	symptomatic relief	6	6	5	5	2	2	2	2	4	3	3	1	3	2	7	5	21	15	1	
39	852098	42	M	buisnessman	no	single	6	1	yes	no	symptomatic relief	5	5	4	4	3	3	2	2	4	2	3	2	3	2	8	6	23	17	2	
40	852120	26	F	home maker	no	single	4	1	no		cosmetic relief	6	6	5	5	4	3	2	2	4	2	2	2	3	2	8	5	23	16	1,2	
41	849629	45	M	retired govt employee	no	single	1	1	yes	yes	symptomatic relief	7	6	6	5	3	3	2	2	4	2	2	1	2	2	7	6	20	16	1	
42	849805	36	F	home maker	no	single	1	1	no		cosmetic relief	8	7	7	6	3	2	2	2	4	3	3	2	3	2	8	5	23	16	1,2,3	hypopigmentation
43	852061	59	F	home maker	no	single	2	1	no		cosmetic relief	7	6	6	5	2	2	2	2	4	1	3	2	3	1	8	6	22	14	1	
44	852275	33	M	engineer	no	single	4	1	yes	yes	symptomatic relief	6	5	5	4	3	2	2	2	4	2	3	2	3	2	9	6	24	16	1	
45	852400	47	M	buisnessman	no	single	6	1	no		cosmetic relief	5	5	4	4	3	2	2	2	4	2	3	2	3	2	8	5	23	15	2	
46	852474	13	F	student	no	single	3	3	no		cosmetic relief	5	5	4	4	3	2	2	2	4	2	3	2	2	1	8	6	22	15	2	
47	763108	20	F	student	no	single	3	2	no		cosmetic relief	6	6	5	5	4	2	2	2	4	1	2	1	2	1	9	7	23	14	1	
48	853096	36	M	accountant	no	single	2	2	yes	yes	symptomatic relief	7	6	6	5	3	2	2	2	4	2	3	2	3	2	8	6	23	16	2	
49	853178	22	M	student	no	single	1	2	no		cosmetic relief	8	7	7	6	3	3	2	2	4	3	2	1	2	2	7	5	20	16	1	
50	853139	20	F	student	no	single	6	3	yes	yes	symptomatic relief	7	7	6	6	2	2	2	2	4	1	3	2	3	1	8	6	22	14	1,2	
51	851150	40	M	driver	no	single	1	3	yes	yes	symptomatic relief	6	6	5	5	3	2	2	2	4	2	2	2	3	2	9	6	23	16	1	
52	853197	15	M	student	no	single	1	1	no		cosmetic relief	5	5	4	4	4	3	2	2	4	1	3	1	2	2	8	6	23	15	2	
53	853367	33	M	teacher	no	single	6	2	no		cosmetic relief	7	7	6	6	3	2	2	2	4	2	3	2	3	1	8	6	23	15	1,2	
54	853152	41	M	buisnessman	no	single	2	1	no		cosmetic relief	8	7	7	6	2	2	2	2	4	1	4	2	4	2	8	5	24	14	1	
55	853534	22	F	home maker	no	single	6	2	yes	no	symptomatic relief	7	6	6	5	3	3	2	2	4	1	3	2	3	3	7	6	22	17	1	
56	902878	21	F	student	no	single	2	2	no		cosmetic relief	6	6	5	5	4	2	2	2	4	1	2	2	3	2	8	5	23	14	1,2	
57	902924	25	M	student	no	single	1	3	yes	yes	symptomatic relief	7	7	6	6	3	3	2	2	4	2	3	2	4	3	9	6	25	18	1	
58	886337	62	M	buisnessman	no	single	4	1	yes	yes	symptomatic relief	8	8	7	7	2	2	2	2	4	2	3	2	3	2	8	5	22	15	1	

Sl. No	UHID	Age	Sex	Occupation	Family History	Number of Keloids	Site of the Keloid	Size of keloid	Pruritus	Improvement in pruritus after treatment	Reason for Treatment	Pain during treatment				Colour		Finish		Contour		Distortion		Texture		Visual Analogue Scale		MSS Score		Side Effects	Hypo/Hyperpigmentation
												Session 1	Session 2	Session 3	Session 4	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment		
59	900389	21	M	student	no	single	2	1	no		cosmetic relief	7	7	6	6	3	2	2	2	4	1	3	2	4	3	8	6	24	16	1,2	
60	897124	42	F	home maker	no	single	1	1	no		cosmetic relief	6	5	5	4	2	2	2	2	4	1	3	2	3	2	7	5	21	14	1	
61	885062	36	F	teacher	no	single	1	1	no		cosmetic relief	7	7	6	6	3	2	2	2	4	2	3	2	4	2	8	6	24	16	1,2	
62	903450	45	M	farmer	no	multiple	3,4	1	no		cosmetic relief	5	5	4	4	2	2	2	2	4	2	2	1	2	1	9	5	21	13	1	
63	909289	31	F	home maker	no	single	5	1	no		cosmetic relief	6	5	5	4	2	2	2	2	4	2	3	2	3	2	8	5	22	15	1,3	hypopigmentation
64	908765	20	F	student	no	multiple	2,3,6	2	no		cosmetic relief	7	7	6	6	3	3	2	2	4	2	2	2	2	2	9	6	22	17	1,2	
65	909674	30	F	home maker	no	single	2	2	no		cosmetic relief	5	5	4	4	4	3	2	2	4	1	2	1	3	1	9	5	24	13	1	
66	909975	17	M	student	no	single	6	1	yes	yes	symptomatic relief	6	5	5	4	3	3	2	2	4	2	3	2	3	1	9	6	24	16	1,2	
67	909979	23	F	student	no	single	4	3	yes	yes	symptomatic relief	7	7	6	6	4	2	2	2	4	2	3	2	3	2	8	6	24	16	1	
68	906098	42	F	home maker	no	single	1	1	no		cosmetic relief	6	6	5	5	3	2	2	2	4	2	3	2	4	3	9	5	25	16	1,2	
69	58722	20	F	student	no	single	4	1	no		cosmetic relief	7	7	6	6	3	2	2	2	4	1	2	1	2	1	8	6	21	13	1	
70	907606	32	M	cab driver	no	multiple	1,5,6	1	no		cosmetic relief	7	6	6	5	2	2	2	2	4	2	3	2	3	2	9	5	23	15	1	
71	880917	45	M	farmer	no	multiple	1,2,4	1	no		cosmetic relief	6	6	5	5	3	2	2	2	4	2	3	2	3	2	9	6	24	16	1	
72	911687	27	F	home maker	no	single	1	1	no		cosmetic relief	8	7	7	6	4	3	2	2	4	1	2	2	2	1	8	6	22	15	1	
73	894074	14	M	student	no	single	6	1	no		cosmetic relief	6	5	5	4	2	2	2	2	4	2	3	2	3	2	8	5	22	15	1,2	
74	821463	32	F	home maker	no	single	6	1	no		cosmetic relief	7	6	6	5	3	2	2	2	4	1	2	1	2	1	9	4	22	11	1	
75	901853	27	M	student	no	single	4	1	yes	yes	symptomatic relief	5	5	4	4	2	2	2	2	4	2	3	2	3	1	8	5	22	14	1	
76	912438	48	M	buisnessman	no	single	2	1	no		cosmetic relief	6	5	5	4	3	2	2	2	4	2	3	2	3	2	8	4	23	14	1	
77	912203	18	M	student	no	single	4	1	yes	no	symptomatic relief	9	8	8	7	2	2	2	2	4	2	3	1	3	2	9	5	23	14	1	
78	912473	31	F	home maker	yes	single	1	1	no		cosmetic relief	6	5	5	4	3	2	2	2	4	2	3	1	3	2	8	6	23	15	1	
79	944962	32	M	construction worker	no	multiple	1,3,4	1	yes	yes	symptomatic relief	5	5	4	4	2	2	2	2	4	1	3	1	3	2	9	6	23	14	1,2	
80	844964	45	F	home maker	no	single	1	2	no		cosmetic relief	6	6	5	5	3	2	2	2	4	2	3	2	3	2	8	5	23	15	2	
81	844969	28	F	home maker	no	single	2	1	no		cosmetic relief	7	7	6	6	3	2	2	2	4	2	2	2	2	1	8	6	21	15	2	
82	843054	34	M	accountant	no	single	2	1	no		cosmetic relief	6	6	5	5	3	2	2	2	4	1	3	1	3	2	9	5	24	13	1,2	
83	843176	29	M	factory worker	no	single	1	2	yes	yes	symptomatic relief	5	5	4	4	3	3	2	2	4	2	3	2	3	1	8	6	23	16	2	
84	843177	15	M	student	no	single	4	1	no		cosmetic relief	6	6	5	5	4	3	2	2	4	1	3	2	3	2	9	5	25	15	1	
85	844953	27	M	construction worker	no	multiple	3,4,6	2	yes	yes	symptomatic relief	6	5	5	4	3	3	2	2	4	2	3	2	3	2	9	6	24	17	1	

Fractional CO2 LASER with Topical Betamethasone																																			
Sl. No.	UHID	Age	Sex	Occupation	Family History	Number of Keloids	Site of the Keloid	Size of keloid	Pruritus	Improvement if pruritus after treatment	Reason for Treatment	Pain during Treatment				Colour		Finish		Contour		Distortion		Texture		Visual Analogue Scale		MSS Score		Side Effects	Hypo/Hyperpigmentation
												Session 1	Session 2	Session 3	Session 4	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment		
1	511033	38	F	home maker	no	single	1	1	no		cosmetic relief	3	3	2	2	3	2	2	1	4	1	3	2	4	2	6	3	22	11	3	Hyperpigmentation
2	606814	39	M	factory worker	no	single	2	2	no		cosmetic relief	4	4	3	3	2	2	2	2	4	2	3	2	3	2	7	4	21	14		
3	621066	32	M	driver	no	single	3	1	no		cosmetic relief	3	2	2	1	3	2	2	2	4	2	3	2	3	2	7	5	22	15		
4	624914	34	F	home maker	yes	single	2	1	no		cosmetic relief	2	2	1	1	2	2	2	1	4	2	3	2	3	2	8	4	22	13		
5	606906	36	F	teacher	no	single	1	1	no		cosmetic relief	3	2	2	1	3	2	2	2	4	2	2	2	3	2	9	4	23	14		
6	589908	37	F	home maker	no	single	1	1	no		cosmetic relief	4	3	3	2	4	2	2	1	4	1	2	2	2	1	8	5	22	12		
7	852726	30	M	factory worker	no	single	3	1	no		cosmetic relief	3	3	2	2	3	2	2	2	4	2	3	2	3	2	7	3	22	13	3	Hyperpigmentation
8	860842	20	M	student	no	single	2	1	no		cosmetic relief	2	2	1	1	2	2	2	2	4	2	2	1	3	2	8	4	21	13		
9	862221	21	M	student	no	single	1	1	no		cosmetic relief	3	3	2	2	3	2	2	1	4	2	3	3	2	1	8	3	22	12		
10	862449	45	F	home maker	no	single	5	1	no		cosmetic relief	4	4	3	3	4	2	2	2	4	1	3	2	3	2	8	4	24	13		
11	862949	27	F	home maker	no	single	1	1	no		cosmetic relief	3	3	2	2	3	2	2	2	4	3	3	2	4	2	9	5	25	16	3	Hyperpigmentation
12	735507	14	F	student	no	single	4	1	no		cosmetic relief	5	4	4	3	2	1	2	2	4	2	2	1	3	2	7	4	20	12		
13	735496	16	F	student	no	single	5	1	no		cosmetic relief	4	3	3	2	3	2	2	1	4	1	3	2	3	1	8	3	23	10		
14	764678	24	M	student	no	single	1	1	no		cosmetic relief	3	3	2	2	2	1	2	2	4	2	2	2	4	2	6	3	20	12		
15	790442	14	M	student	no	single	3	1	no		cosmetic relief	2	2	1	1	3	2	2	1	4	2	3	2	3	2	7	4	22	13	3	Hyperpigmentation
16	874279	26	M	student	no	single	6	1	no		cosmetic relief	3	2	2	1	2	2	2	2	4	2	3	2	3	2	8	5	22	15		
17	890669	20	F	student	yes	single	2	1	no		cosmetic relief	4	3	3	2	3	2	2	1	4	1	2	2	4	3	7	4	22	13		
18	565089	36	F	home maker	no	single	1	1	no		cosmetic relief	3	3	2	2	2	2	2	1	4	3	2	1	3	2	8	3	21	12		
19	582445	44	M	factory worker	no	multiple	4,5,6	2	no		cosmetic relief	4	3	3	2	4	2	2	2	4	2	4	3	4	1	9	4	27	14		
20	839716	54	M	buisnessman	no	single	3	2	no		cosmetic relief	5	4	4	3	4	3	2	2	4	2	2	1	3	2	8	5	23	15	3	Hyperpigmentation
21	401827	36	F	home maker	no	single	5	1	no		cosmetic relief	4	4	3	3	3	2	2	2	4	1	3	2	2	1	7	3	21	11		
22	532311	37	F	home maker	no	single	1	2	no		cosmetic relief	3	3	2	2	3	2	2	1	4	1	2	1	3	2	8	4	22	11		
23	596287	34	F	home maker	no	single	2	1	no		cosmetic relief	4	3	3	2	2	1	2	2	4	2	3	2	4	3	8	3	23	13		
24	517212	47	M	farmer	no	single	6	1	no		cosmetic relief	3	2	2	1	3	2	2	1	4	1	3	2	3	2	7	3	22	11		
25	506725	34	M	engineer	no	single	6	2	no		cosmetic relief	2	2	1	1	3	2	2	1	4	2	3	2	3	2	8	4	23	13		
26	505595	46	F	home maker	no	single	1	1	no		cosmetic relief	3	3	2	2	2	2	2	1	4	2	2	2	4	1	8	3	22	11	3	Hyperpigmentation
27	840537	45	M	factory worker	no	single	3	1	no		cosmetic relief	4	3	3	2	2	1	2	1	4	1	3	2	2	1	9	4	22	10		
28	849877	35	M	bank manager	no	single	2	1	no		job purpose	4	4	3	3	3	2	2	1	4	2	3	2	3	1	7	3	22	11		
29	846374	52	M	buisnesman	no	single	4	1	no		cosmetic relief	3	2	2	1	3	2	2	1	4	2	3	2	2	1	8	4	22	12		
30	850775	57	F	home maker	no	single	4	1	no		cosmetic relief	2	2	1	1	3	2	2	1	4	2	3	2	3	2	9	3	24	12	3	Hyperpigmentation
31	898052	32	M	buisnessman	no	single	1	1	no		cosmetic relief	3	3	2	2	2	2	2	1	4	2	3	2	3	2	8	4	22	13		
32	903147	40	M	driver	no	single	1	1	no		job purpose	4	3	3	2	3	2	2	1	4	1	3	2	2	1	9	3	23	10		
33	901354	25	F	home maker	yes	single	2	1	no		cosmetic relief	3	3	2	2	3	2	2	2	4	1	3	2	3	2	8	4	23	13		
34	903187	25	F	student	no	single	6	1	no		cosmetic relief	4	3	3	2	4	2	2	2	4	2	3	2	3	2	7	3	23	13		
35	903350	21	F	student	no	single	1	1	no		cosmetic relief	3	3	2	2	2	1	2	2	4	2	2	1	4	2	8	3	22	11	3	Hyperpigmentation
36	910757	20	F	student	no	multiple	1,4,6	1	yes	yes	symptomatic relief	4	4	3	3	3	2	2	1	4	2	3	2	3	2	8	4	23	13		
37	910677	35	M	govt emplyee	no	single	1	1	no		cosmetic relief	3	3	2	2	3	1	2	2	4	2	3	2	3	2	9	3	24	12		
38	910679	35	F	home maker	no	single	4	1	no		cosmetic relief	3	3	2	2	2	1	2	1	4	2	4	3	4	2	8	3	24	12		
39	910778	37	F	home maker	no	single	6	1	no		cosmetic relief	4	3	3	2	3	2	2	2	4	1	3	2	3	2	7	4	22	13		
40	902602	38	M	buisnesman	no	single	5	1	no		cosmetic relief	2	2	1	1	2	1	2	1	4	1	2	2	2	1	8	3	20	9		
41	910517	14	F	student	no	multiple	2,4,3,5,6	1	no		cosmetic relief	3	3	2	2	3	2	2	2	4	2	3	2	3	2	9	3	24	13		
42	899890	26	F	home maker	no	single	1	1	no		cosmetic relief	4	3	3	2	4	2	2	2	4	2	4	3	4	2	8	4	26	15		
43	758677	23	M	student	no	single	1	1	no		cosmetic relief	3	3	2	2	3	2	2	2	4	2	3	2	3	2	7	3	22	13		
44	843477	30	M	truck driver	no	single	4	1	no		cosmetic relief	2	2	1	1	3	1	2	2	4	2	2	1	4	2	8	3	23	11		
45	843474	26	F	nurse	no	single	5	3	no		cosmetic relief	3	2	2	1	3	2	2	1	4	1	3	2	3	2	9	3	24	11	3	Hyperpigmentation
46	843453	46	M	factory worker	no	single	3	1	no		job purpose	4	3	3	2	3	2	2	2	4	2	4	3	2	1	8	4	23	14	3	Hyperpigmentation
47	893462	30	M	govt emplyee	no	single	1	3	no		job purpose	3	3	2	2	3	2	2	2	4	2	3	2	3	2	8	3	23	13		
48	843550	40	M	farmer	no	multiple	1,2,4	1	no		cosmetic relief	2	2	1	1	2	2	2	2	4	1	4	3	4	3	8	4	24	15		
49	840726	38	M	buisnessman	no	single	4	1	no		cosmetic relief	3	3	2	2	2	2	2	1	4	2	3	2	3	2	9	4	23	13		
50	652508	16	F	student	no	single	6	1	no		cosmetic relief	4	3	3	2	2	1	2	1	4	2	3	2	3	1	8	3	22	10		
51	836964	60	M	farmer	no	single	1	3	yes	yes	symptomatic relief	3	3	2	2	3	2	2	2	4	1	2	2	4	3	7	4	22	14		
52	613276	35	F	home maker	no	single	1	1	no		cosmetic relief	4	3	3	2	2	2	2	2	4	2	3	2	3	2	8	4	22	14	3	Hyperpigmentation
53	344135	29	M	driver	no	single	6	1	yes	yes	symptomatic relief	5	5	4	4	3	2	2	2	4	2	4	3	3	2	9	3	25	14		
54	819894	28	F	home maker	no	multiple	1,2,4,5	3	no		cosmetic relief	4	4	3	3	3	2	2	2	4	2	3	2	4	3	8	5	24	16		
55	735234	48	M	farmer	no	multiple	1,3,5	2	no		cosmetic relief	3	3	2	2	3	2	2	1	4	1	2	1	3	2	8	4	22	11		
56	844195	30	F	home maker	no	multiple	4,5,6	2	no		cosmetic relief	4	3	3	2	3	2	2	1	4	2	3	2	3	2	7	3	22	12	3	Hyperpigmentation
57	826216	11	F	student	no	multiple	1,2,3,5	3	yes	yes	symptomatic relief	3	3	2	2	2	2	2	2	4	1	3	2	2	2	8	4	21	13	3	Hyperpigmentation
58	786326	50	F	home maker	no	single	4	2	no		cosmetic relief	2	2	1	1	4	3	2	2	4	1	3	2	3	2	9	3	25	13		
59	530781	43	M	construction worker	no	single	2	3	yes	no	symptomatic relief	3	3	2	2	3	2	2	1	4	1	4	3	4	3	8	4	25	14		
60	840946	49	F	home maker	no	single	1	1	no		cosmetic relief	4	3	3	2	4	3	2	2	4	2	3	2	2	1	7	3	22	13		
61	892749	19	M	student	yes	single	1	3	yes	yes	symptomatic relief	5	4	4	3	2	2	2	2	4	1	2	1	3	1	8	4	21	11		
62	903347	21	F	student	no	single	2	3	no		cosmetic relief	4	4	3	3	2	2	2	2	4	2	3	2	4	3	9	4	24	15	3	Hyperpigmentation
63	735496	16	F	student	no	single	5	1	no		cosmetic relief	3	3	2	2	3	2	2	1	4	1	4	3	3	1	8	3	24	11		
64	923699	33	F	home maker	no	single	6	1	no		cosmetic relief	4	4	3	3	3	2	2	2	4	2	4	3	3	2	7	4	23	15		
65	850779	50	M	farmer	no	single	2	3	yes	yes	symptomatic relief	5	4	4	3	2	1	2	1	4	2	3	2	3	2	9	4	23	12		
66	826616	31	M	teacher	no	single	6	3	yes	yes	symptomatic relief	4	4	3	3	3	2	2	2	4	1	2	2	4	3	8	4	23	14		
67	848843	22	M	student	no	single	4	1	no		cosmetic relief	3	3	2	2	2	2	2	1	4	2	4	3	3	2	7	3	22	13		
68	85096	21	F	student	no	single	1	3	no		job purpose	3	3	2	2	3	2	2	1	4	2	3	2	3	2	8	3	23	12		
69	849904	25	M	student	no	single	4	1	no		cosmetic relief	4	3	3	2	3	2	2	1	4	2	2	2	3	2	9	4	23	13	3	Hyperpigmentation
70	789291	40	F	home maker	no	single	1	2	no		cosmetic relief	2	2	1	1	2	1	2	1	4	2	3	2	3	2	8	3	22	11		
71	851128	21	M	student	no	single	1	2	yes	yes	symptomatic relief	3	3	2	2	3	2	2	2	4	2	3	2	3	1	7	4	22	13		

Sl. No.	UHID	Age	Sex	Occupation	Family History	Number of Keloids	Site of the Keloid	Size of keloid	Pruritus	Improvement if pruritus after treatment	Reason for Treatment	Pain during Treatment				Colour		Finish		Contour		Distortion		Texture		Visual Analogue Scale		MSS Score		Side Effects	Hypo/Hyperpigmentation
												Session 1	Session 2	Session 3	Session 4	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment		
72	850483	46	F	home maker	no	single	1	2	no		cosmetic relief	4	3	3	2	3	2	2	2	4	2	2	1	2	2	8	3	21	12		
73	850349	30	M	govt emplyee	no	single	6	2	yes	yes	symptomatic relief	3	3	2	2	2	2	2	2	4	2	3	2	3	1	9	4	23	13		
74	843058	39	M	farmer	no	single	6	1	no		cosmetic relief	2	2	1	1	2	1	2	1	4	1	4	3	3	2	8	3	23	11		
75	845581	21	M	student	yes	multiple	1,3,4	1	no		cosmetic relief	3	3	2	2	3	2	2	1	4	2	3	2	3	1	7	4	22	12		
76	850215	33	M	farmer	no	multiple	2,6	3	yes	yes	symptomatic relief	4	3	3	2	3	2	2	2	4	2	3	2	2	2	8	4	22	14		
77	850715	20	F	student	no	single	4	3	yes	yes	symptomatic relief	3	3	2	2	3	2	2	1	4	1	2	2	2	2	8	3	21	11	3	Hyperpigmentation
78	904017	49	F	home maker	no	single	1	1	no		cosmetic relief	2	2	1	1	2	2	2	1	4	2	3	2	2	1	8	4	21	12		
79	816150	37	F	home maker	no	single	4	1	no		cosmetic relief	4	3	3	2	2	2	2	2	4	1	2	1	3	2	9	3	22	11		
80	845063	38	M	farmer	no	multiple	1,3,4	3	yes	no	symptomatic relief	3	3	2	2	3	2	2	2	4	1	3	2	2	1	8	4	22	12		
81	845514	24	M	buisnessman	no	single	2	1	no		cosmetic relief	2	2	1	1	2	2	2	1	4	2	2	2	3	2	8	3	21	12		
82	845515	25	M	student	no	single	2	1	yes	yes	symptomatic relief	3	3	2	2	3	2	2	2	4	2	3	2	3	2	9	4	24	14		
83	844601	42	M	buisnessman	no	single	1	1	yes	yes	symptomatic relief	4	3	3	2	4	2	2	1	4	2	3	2	3	2	8	3	24	12		
84	769262	39	F	home maker	no	single	4	2	no		cosmetic relief	3	3	2	2	2	1	2	2	4	1	3	2	4	3	9	4	24	13		
85	844896	27	F	home maker	no	multiple	3,4,6	1	no		cosmetic relief	2	2	1	1	3	2	2	1	4	2	2	2	3	1	8	3	22	11	3	Hyperpigmentation
				Size of Keloids : 1 - <2cm 2 - 2-5cm 3 - >5cm			SITE OF LESION : (1)MID STERNUM (2)EAR LOBE (3) ARM (4)SHOULDER (5)LEGS (6) OTHERS				Side Effects - 1 - Telengectasia 2 - Skin Atrophy 3 - Pigmentary Changes (Hypo/Hyperpigmentation)																			