“EFFICACY AND SAFETY OF PLATELET RICH PLASMA(PRP) FOR TREATMENT OF ACNE SCARS.”

This dissertation is submitted to

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY

In partial fulfillment of the requirement of the award for the degree of

M.D BRANCH XX

DERMATOLOGY, VENEREOLOGY AND LEPROSY

STANLEY MEDICAL COLLEGE

CHENNAI – 600 001

APRIL 2015

DECLARATION

I solemnly declare that the dissertation titled "***EFFICACY AND SAFETY OF PLATELET RICH PLASMA (PRP) FOR TREATMENT OF ACNE SCARS***" was done by me at **Government Stanley Medical College and Hospital during 2012-2015** under the guidance and supervision of my Head of Department **Dr. V. Anandan, M.D.**

The dissertation is submitted to **THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY** towards the partial fulfillment of requirement for the award of **M.D. Degree (Branch XX) in DERMATOLOGY, VENEREOLOGY & LEPROSY.**

Place:

Date: Signature

CERTIFICATE

Certified that this dissertation entitled **"*EFFICACY AND SAFETY OF PLATELET RICH PLASMA (PRP) FOR TREATMENT OF ACNE SCARS*"** is a bonafide work done by **Dr. SHUBHRA SHUKLA** post Graduate Student of the Department of Dermatology, Venereology and Leprosy, Stanley Medical College, Chennai – 600 001 during the academic Year 2012 – 2015. This work has not been submitted previously for the award of any degree.

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ACKNOWLEDGEMENT

It is with immense pleasure and gratitude that I thank ***Dr. AL. MEENAKSHI SUNDARAM, M.D., D.A., DEAN, GOVERNMENT STANLEY MEDICAL COLLEGE & HOSPITAL*** *for bestowing on me the permission and privilege of presenting this study and for enabling me to avail the institutional facilities.*

I am gratefully indebted to ***Dr. V. ANANDAN, M.D.,*** *Head of Department of Dermatology and Leprology for his invaluable guidance and motivation. Without his constant support, it would not have been possible to complete this study.*

I am grateful to ***Dr. A. RAMESH, M.D., D.D., D.N.B.,*** *Additional professor of Dermatology for his support and encouragement.*

I duly acknowledge the invaluable role played by Dr. P. Elangovan, M.D, Professor and Head of Department of Venereology and Dr.S.Thilagavathy, M.D, D.V, Professor of Venereology, through their constant support and motivation.

Words will not suffice the gratitude I owe to my beloved guide Dr. Mani Surya Kumar M.D, Assistant Professor, Department of Dermatology, for his guidance and endless patience in molding of the study.

I am sincerely grateful to Dr. G.R. Ratnavel M.D, Professor and Head of Department of Cosmetology, for his cooperation and valuable advice.

I would like to extend my thanks to all the Assistant Professors, Dr.K.P.Saradha, Dr. K. Rajkumar, Dr. B.K. Aarthi , Dr. Sowmiya, Dr. Senthil Kumar, Dr.MohanaSundari, Dr. Jayanthi, Dr. Vanathi, Dr. Amutha, Dr.Kayalvizhi, Dr.Chithra and Dr. Ranjini, for their enthusiasm and painstaking efforts to materialize this study.

I am inclined to express my gratitude to Late Dr. R. Shantharaman, M.D, D.D, Former Senior Assistant Professor, Department of Dermatology, for his valuable suggestions and constant inspiration. May his soul rest in peace.

I wholeheartedly thank my colleagues for their constant help and favors. I also acknowledge the help provided by the paramedical staff.

A sincere thanks to all my patients for their cooperation & participation in this study.

Last but not the least I thank my parents and the Almighty God whose blessings are always with me.

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CONTENTS

Efficacy And Safety of PLATELET RICH PLASMA (PRP) for treatment of acne scars

ABSTRACT

Key words: Acne scars, Platelet rich Plasma

INTRODUCTION:

Acne scarring can produce severe disfigurement of face. Scarring is a complex biological process that involves various chemical mediators, extracellular matrix, parenchymal resident cells and infiltrating blood cells.

Autologous PRP has been found to stimulate fibroblast growth and therefore helps in scar healing. Modern technology allows us to concentrate platelets and white blood cells from a patient's blood (autologous therapy) and to induce the release of growth factors by injecting the solution directly into injured tissue, stimulating the same healing process but in a more directed form.

METHODS AND MATERIALS:

Forty patients of atrophic acne scars attending Dermatology OPD in Govt. Stanley Hospital during period from JUNE 2013 to MAY 2014 were selected. After brief & relevant medical history and physical examination, acne scars were graded. Informed consent and digital photographs of face were taken. PRP was injected by multiple tiny punctures under the dermis under topical anesthesia. Up to 6 sittings, 4 weeks apart were given within a 6-month time frame. At the end of treatment duration, scars were graded using grading system as used in the beginning, photographs taken and compared.

OBSERVATIONS:

Marked improvement was seen in 42.5 % patients while 35% patients showed moderate improvement. In maximum patients improvement became visible at the end of 3rd sitting. Patient satisfaction was good in 52.5% patients and very good in 27.5 % cases. There was a good reduction in DLQI too (61.13 % improvement).Complications seen were only in form of transient erythema and pain.

CONCLUSION:

Marked to Moderate improvement was seen in most cases, which is comparable with other modalities used for management of acne scars. It does not hamper daily activity of the patient as it is performed as out-patient procedure. To conclude Platelet rich plasma therapy is easy to perform and provides satisfactory results and that too with minimum side effects.

INTRODUCTION

Acne is a disease of pilosebaceous unit, most commonly affecting adolescents, clinically characterized by pleomorphic variants of lesions like papules, pustules, comedones, nodules and cysts . It is in most cases a self-limiting disease. It is however associated with variable amount of scarring, so there can be life long sequelae in form of atrophic or hypertrophic scar formation. In some patients, the scarring is minimal, however in some scarring may be severe.The cause of this scarring is basically defective wound healing.

Scars resulting from acne may be of following types:

1) Ice pick scars
2) Rolling scars
3) Box car scars
4) Hypertrophic scars
5) Perifollicular elastolysis
6) Perifollicular fibrosis
7) Atrophic macules.

Different types of scars may be present in a same patient. Management of acne scars usually involves combination of different modalities.

Various methods in use for acne scar management are:

1) Use of topical agents like tretinoin, steroids.

2) Punch elevation, Punch graft.

3) Subcision

4) Microdermabrasion

5) Dermabrasion

6) Lasers

7) Fillers

Apart from these conventional procedures, use of Platelet Rich Plasma (PRP) for acne scars is gaining popularity. PRP, in which the platelets are in highly concentrated form has shown its effect in accelerating tissue repair & wound healing. It therefore holds a role in treatment of acne Scars. It can be used either alone or in combination with other methods. The scarring in acne occurs due to defective tissue healing after the inflammation occurring during the disease process. The platelets release a variety of growth factors including Transforming Growth Factor, Fibroblast Growth Factor and Vascular Endothelial Growth Factor.

These factors have the potential to bring about tissue re-modelling by regulating cell migration, proliferation, differentiation and extra cellular matrix accumulation. Autologous PRP is a latest advancement, a more natural procedure, in which the platelets extracted from one's own blood are re-injected into the body, into the area where the effect is desired so that the platelets carry out the function in a more directed way.

ACNE

HISTORY

ACNE is not a disease of modern age alone. The First description of acne can be found in the Sushrut Samhita under Kshudra Roga as Mukha Dushika. Mentions are found in ancient Egyptian writings about this condition in the Pharaoh and various treatments used by them. Some sources say that it was Emperor Justinian's physician, Aetius Amidenus, who used the word 'ACNE'or the first time during sixth century A.D. Word ACNE comes from word 'AKME'. It is actually corrupt form of the word AKME, which means 'PRIME OF LIFE'[1].

REVIEW
OF LITERATURE

EPIDEMIOLOGY

Acne vulgaris, also called as ‘pimples’, by common people is a universal disease affecting about 9.4% population globally[2]. Around 90% people get affected in their teens & in some it persists till adulthood. In India prevalence rate is about 50.60% in males and 38.13% in females, in age group of 12-17 years[3]. However its sequel that is scarring continues in adulthood.

Difference in male and female prevalence is often reported, but it is more due to social biasing. Studies have also shown difference in the prevalence of acne in rural and urban areas[4].

It is believed to be more common in urban population, suggesting the role of lifestyle and diet in the occurrence of acne.Around 20 % have severe acne which can result in permanent physical as well as mental scarring.

DEFINITION

Acne is a self-limiting inflammatory disease of pilosebaceous units seen predominantly in adolescents, characterised by seborrhoea & pleomorphic lesions like open and closed comedones, erythematous papules, pustules, nodules, cysts and in many cases scarring will ensue

which can be either mild or severe, depending upon the degree of inflammation[5].

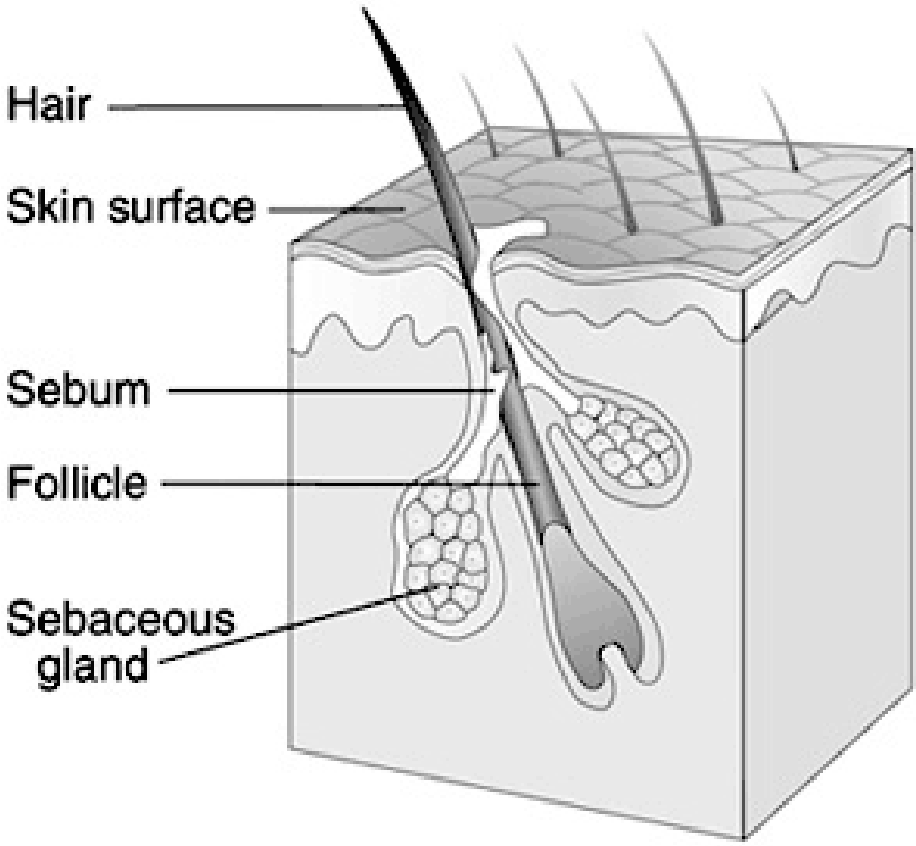
The condition is most common between 12-25 years. Acne is undoubtedly one of the most common conditions encountered by the Dermatologists.

ETIOPATHOGENESIS

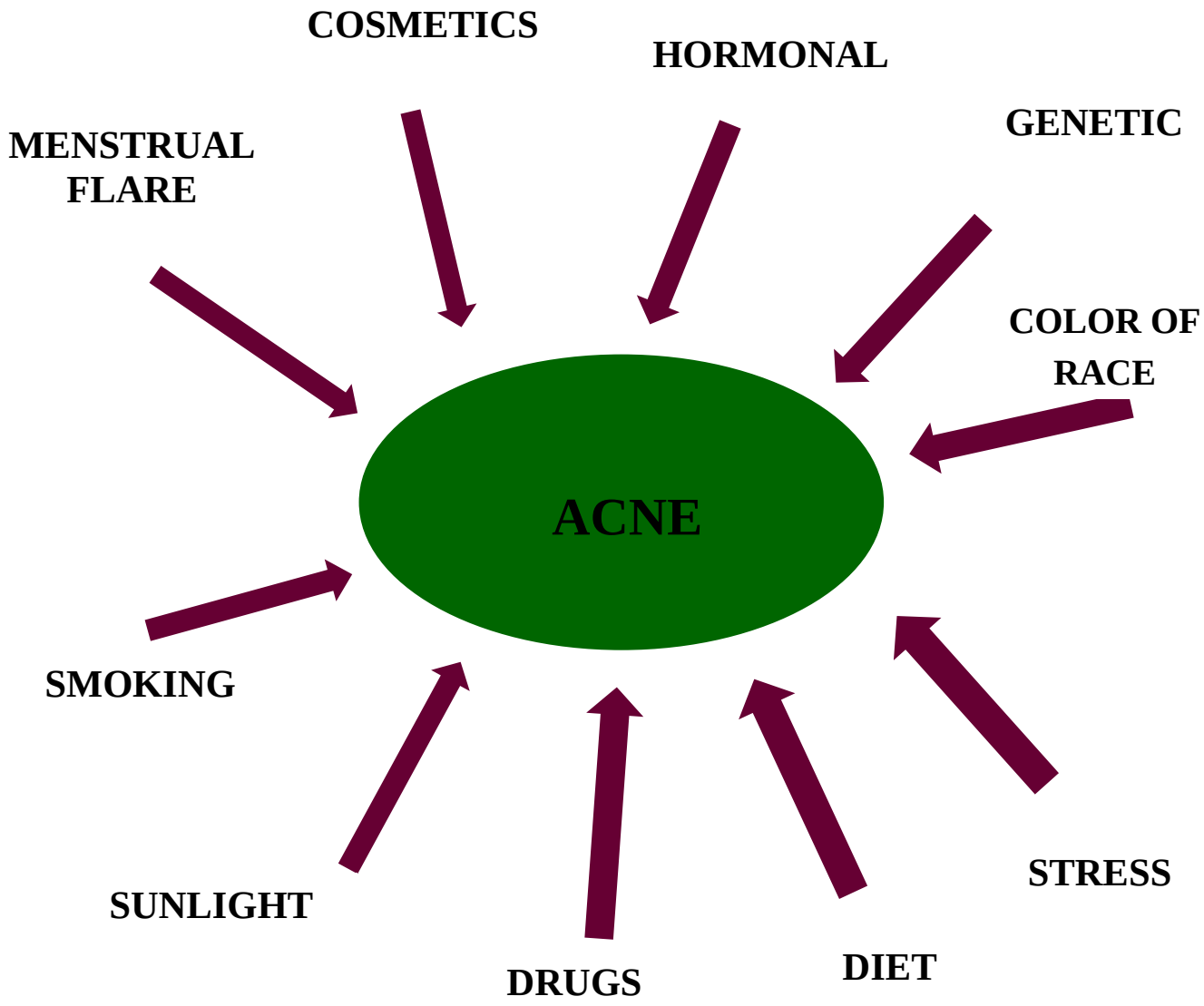
SEBACEOUS GLANDS AND SEBUM:

Sebaceous gland is a holocrine gland. They occur over most of the body, but not normally over palms and soles and sparsely over the dorsum of hands and feet. Sebaceous glands are largest and most numerous on face, scalp, upper trunk, external auditory meatus and anogenital surfaces.

There are between 400-900 glands/ cm^2 over scalp, forehead, face and chin[6]. At other places they are less than 100glands /cm^2. Sebaceous glands are active in newborn, but later they involute and become non-functional until puberty. Sebum is a complex mixture of lipids, consisting of glycerides, free fatty acids, wax esters, squalene, cholesterol esters and cholesterol. Sebum is fungistatic.


Hair
Skin surface
Sebum
Follicle
Sebaceous gland

PRECIPITATING /AGGRAVATING FACTORS FOR ACNE



PRECIPITATING OR AGGRAVATING FACTORS

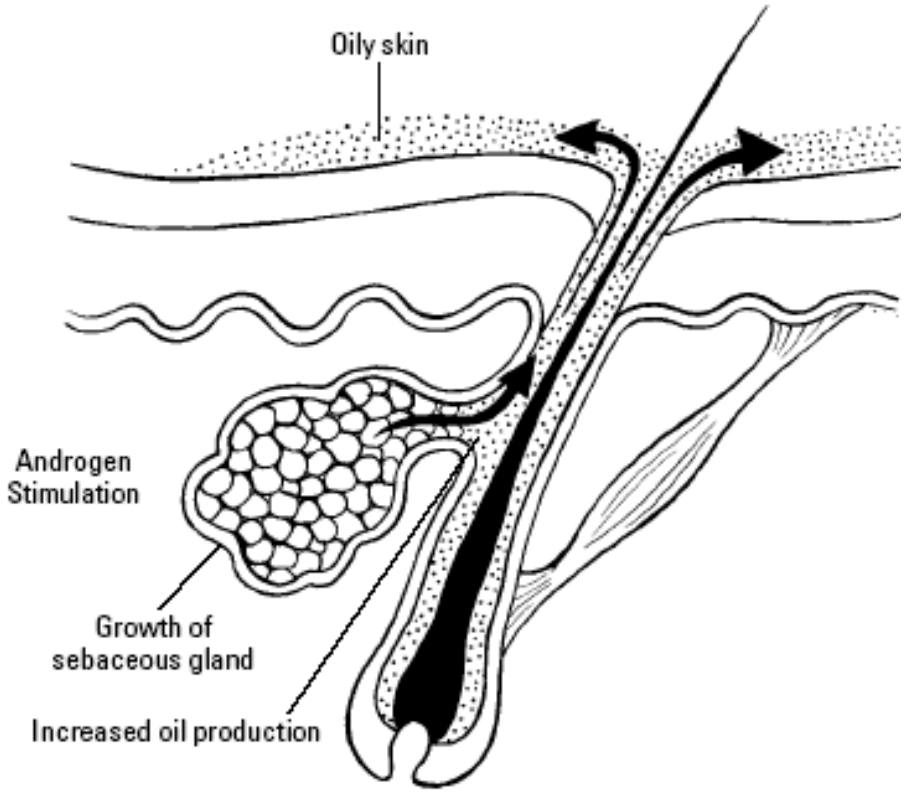
1) Hormonal

Periods of excessive hormonal activity, such as menstrual cycles and puberty, may contribute to the formation of acne. An increase in androgens during puberty causes enlargement of follicular glands and increased sebum production. Similar effect is shown by use of anabolic steroids. It has also been seen that acne develop earlier in females than males, which may be due to earlier onset of puberty in girls. Hormones linked to acne are: the androgens[7] testosterone, dihydrotestosterone (DHT) and dehydroepiandrosterone sulfate (DHEAS), as well as insulin-like growth factor 1 (IGF-I).

Late onset acne is not common. Acne vulgaris in an adult women can be due to any underlying condition such as pregnancy, polycystic ovary syndrome, hirsutism, or Cushing's syndrome.

Acne climacterica :

It is Menopause associated acne which occurs as the production of the natural anti-acne ovarian hormones estradiol and progesterone fails, permitting the unopposed action of the acnegenic hormone testosterone.



2) Genetics

Positive family history has been seen in patients with severe persistent acne.[8] In monozygotic twins sebum excretion rate is same.The genetics of acne susceptibility is most likely polygenic, as the disease does not follow classic Mendelian inheritance pattern.

3) Cosmetics

Heavy use of cosmetics can cause flare up of acne. It may be due to blocking of the pilosebaceous orifices by the chemicals. External application of oil, pomades (pomade acne) etc. can cause acne.

4) Sweating

Acne patients usually notice aggravation of acne by sweating. Hot and humid climate aggravates acne, due to increased sweating which causes ductal hydration[9].

5) Menstrual flare

Premenstrual flare is probably due to altered hydration of pilosebaceous epithelium[10].

6) Sunlight

There is no scientific evidence that sunlight improves acne, the improvement seen may be due to the cosmetic effect of tanning .

7) Stress

There exists a ‘stress-acne-stress’ cycle. Stress causes deterioration of acne. Acne itself causes stress. Under stress, body secretes stress hormone Cortisone, which causes increased production of testosterones, resulting in sebaceous gland stimulation and paving way for acne formation. Patients meddling with the lesions further causes aggravation of lesions.

8) Smoking

Causes exacerbation of acne. Smoke contains polycyclic aromatic hydrocarbons and arachidonic acid, which induce phospholipase A dependent inflammatory pathway[11]. Smokers also consume diet containing high saturated fat and lower polyunsaturated, linoleic acid compared to those who do not smoke.

9) Diet

Foods with high glycemic index, milk products, sweets, chocolates are known to exacerbate acne. They cause hyperinsulinemia leading to increased androgen synthesis[12] .

10) Drugs

Steroids, anticonvulsants, isoniazid, pyrazinamide, lithium, risperidone, vitamin B12 are known to induce acne like eruptions.

11) Racial Differences

Although acne affects all population, few racial differences are known. Japanese are said to be less affected than Americans. Also cystic acne is more common among the Whites.

PATHOGENESIS OF ACNE

Pathogenesis of acne vulgaris is multifactorial. Main factors involved are:

1) Seborrhoea

2) Ductal hyperproliferation

3) Propionibacterium acnes colonization

4) Inflammation

SEBORRHOEA

Excess sebum production is a pre-requisite for acne formation[13]. The level of sebum production correlates well with the severity of acne. This Sebaceous activity is under the control of androgens, which can be of gonadal or adrenal origin. In androgen insensitive subjects, there are no androgen receptors, there is no sebum production and no acne develop. The Dehydroepiandrosterone sulphate is converted to Dihydrotestosterone (DHT)and this binds to sebocyte resulting in excess sebum production anddevelopment of comedones in acne prone persons. Androgens regulate function by binding to nuclear androgen receptors (ARs) present in the sebaceous gland.

Dehydroepiandrosterone sulphate (DHEAS)

Dihydrotestosterone (DHT)

Nuclear Androgen Receptors(AR) over sebocytes

Increased sebum production

Changes in the ductal microenvironment

Acne

Androgen effects on the pilosebaceous unit are reasonably well documented. Testosterone and DHT act through a single nuclear androgen receptor, with dihydrotestosterone (DHT) as the most active ligand. Sebum excretion varies from follicle to follicle. In acne patients, there is marked variation in individual follicular sebum excretion. This hypothesizes that certain follicles may be prone to acne and that an

enhanced peripheral (end organ) response to androgens is a probable factor. Weak prohormones (DHEA, DHEAS and androstenedione) only act after conversion to more potent androgens testosterone and 5α-DHT. Sebaceous glands in some areas show abnormally high 5α-reductase activity. In addition, abnormally high levels of plasma DHT and urinary 5α-androstanediols, considered to be biological markers of cutaneous androgen metabolism. This has been identified in some female acne patients. Androgen action on the sebaceous gland may be independent of serum hormone levels.

There are two forms of 5α-reductase. 5α-reductase type-I is the most relevant in acne supported by the fact that Finasteride, an inhibitor of type II 5α-reductase, does not reduce sebum production and the fact that patients with a deficiency of type II 5α-reductase have normal sebum levels. Regional differences in the activity of type I 5α-reductase in isolated sebaceous glands from various body sites also support the end-organ hyper-responsiveness theory for acne.

Mechanism for increased sebum production under androgen effect

- Excess androgen production
- Increased free circulating androgens which may be accompanied by relative reduction of sex hormone binding globulin (SHBG).

- Increased response of target cells
- Increased capacity of receptors to bind androgens.

Sampling from skin surface lipids has shown that patients with acne tend to have higher level of squalene and wax esters, while fatty acids are at lower levels. Linoleic acid is significantly reduced in epidermal and comedonal lipids, relating with ductal hyperproliferation.

DUCTAL HYPERPROLIFERATION

The infundibular portion becomes hyperkeratotic .The stimulus to this hyperkeratosis may be androgens or due to the irritating effect of sebaceous lipids. Also there is increased cohesion of keratinocytes.This leads to formation of a plug in follicular ostia in which bacteria, sebum, keratin gets accumulated. As a result there is dilatation of follicle leading to microcomedone formation. Several factors have been implicated in inducing keratinocyte hyperproliferation. These include sebaceous lipid composition, androgens, cytokines produced locally andbacteria.Among abnormal sebaceous lipids, linoleic acid levels are of importance. Among the cytokines produced by keratinocytes, levels of IL-1- alpha are important pathologically[14].

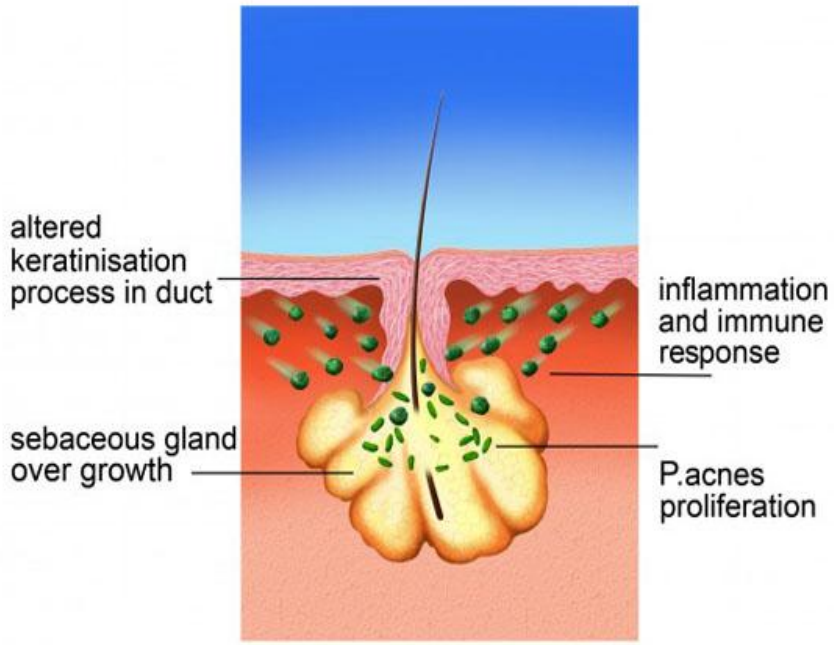
Certain externally applied chemicals present in cosmetics like isopropyl myristate and propylene glycol may also contribute to comedogenesis.

PROPIONIBACTERIUM ACNES COLONIZATION

Acne is not an infectious disease. But in case of inflammatory acne, the blocked pilosebaceousduct may get infected with P. acnes when it gets trapped in the cornified plugs within the ducts. Propionibacterium acnes causes production of proinflammatory cytokines (like IL-8 & Human –beta-defensin-2) by binding through Toll like receptors[15] .They are responsible for breakdown of triglycerides to free fatty acids which leads to follicular hyperkeratosis. It also produces other chemotactic and proinflammatory substances. Powerful hydrolytic enzymes levels rise, making tissue damage inevitable.

TOLL LIKE RECEPTORS:

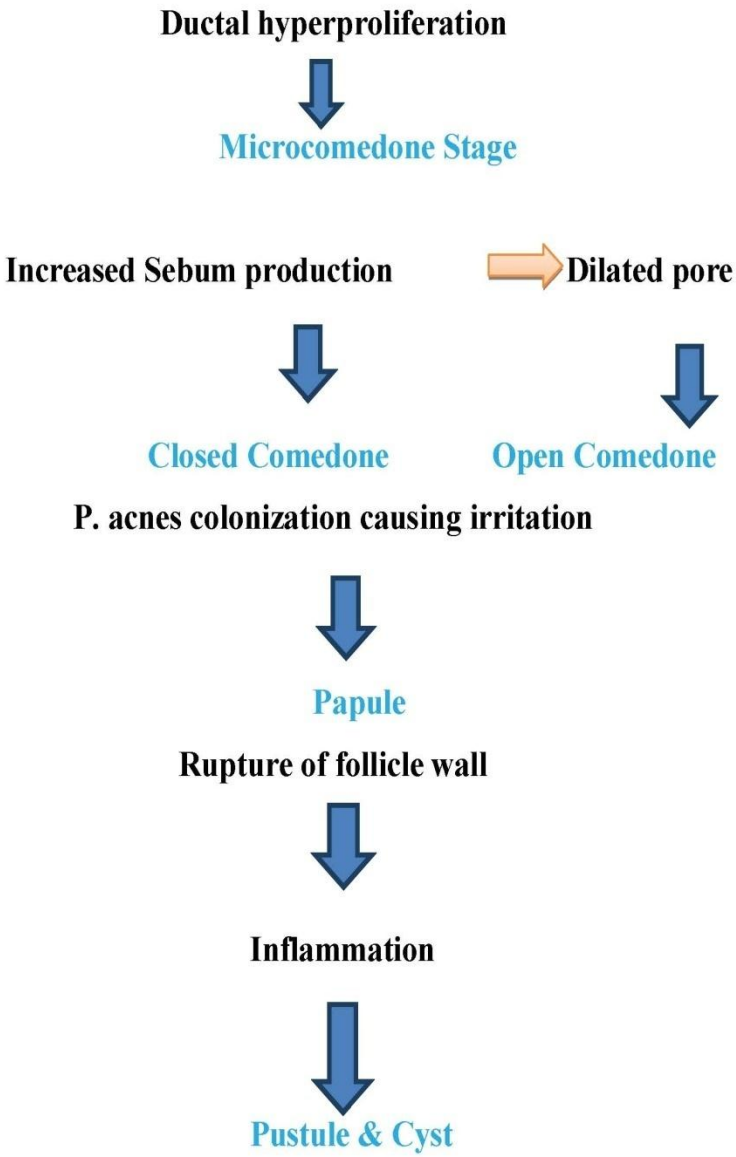
These are a class of proteins which play important role in body's innate immunity. They are actually a type of pattern recognition receptor. Thirteen TLRs have been identified in humans. P. acnes activates TLR-2 on keratinocytes and monocytes thus causing production of pro-inflammatory cytokines.



INFLAMMATION

It is the major cause of scarring. Linoleic acid, which is known to be deficient in acne, could lead to an alteration in the integrity of the barrier function within individual follicles[16]. Basement membrane of the follicle wall remains intact in uninvolved follicles. An unknown soluble

antigen could be a trigger for inflammation. Inflammation up regulates sebum production, in genetically predisposed individuals, which elaborates IL-1 alpha initiating comedogenesis.



RECENT CONCEPTS:

It has been believed for long that the initial lesion of acne is non – inflammatory. After colonization with P. acnes, due to the innate immune response, the inflammation starts leading to formation of so called inflammatory lesions i.e. papule, pustule or nodule. However recent evidences and studies support that inflammation is present during all the stages of acne, may be sub-clinically, even before comedone formation[17]. The uninvolved skin in acne patients has been found to contain elevated levels of CD3+ and CD4+ T cells in the perifollicular and papillary dermis. Lipoperoxidation brings about modification of sebum composition which can affect keratinocytes proliferation and differentiation. Lipid peroxidation products can induce production of pro-inflammatory cytokines and activation of peroxisome proliferators-activated receptors (PPARs). PPARs are transcription factors involved in control of inflammation.

CLINICAL FEATURES

CONSISTS OF INFLAMMATORY & NON INFLAMMATORY LESIONS. **COMEDONES** are the non- inflammatory lesions - They are the characteristic early lesions.

Types of comedones:

Open comedones- Also known as Black Heads. Dome shaped papules with dilated follicular outlets filled with keratin. The visible black colour is due to melanin deposit.

Closed comedones- Also known as White Heads. Around one mm in diameter, skin coloured and there is no visible follicular opening. They can be visualised properly in adequate light and by stretching the skin.

Submarine comedones- They are larger. Greater than 0.5 cm in diameter. They lie more deeply in skin. They may be the source of recurrent inflammatory nodular lesion.

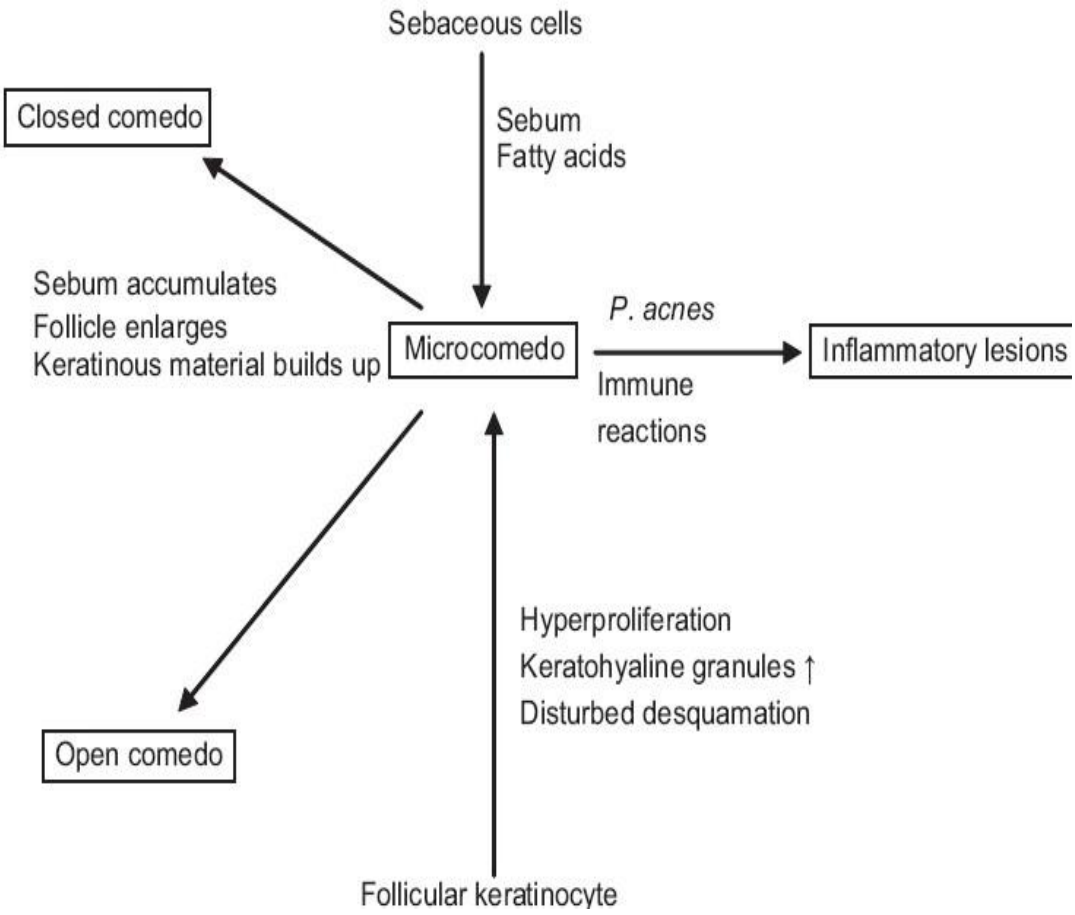
Sandpaper comedones- Multiple, very small white heads, commonly over forehead. There is a rough, gritty feeling on touching.

Secondary comedones – They are caused by exposure to dioxins, pomades, topical steroids.

Inflammatory lesions include superficial lesions like papules and pustules (5 mm or less in diameter) & deep lesions like pustules and deep nodules. Nodules are seen more frequently in males. They may be hemorrhagic or exudative, leading to disfigurement.

When sinuses are formed between pustules and nodules, it leads to devastating cosmetic disfigurement and inevitable scarring[18]. Scarring usually follows deep-seated inflammatory lesions, but may also occur as a result of more superficial inflamed lesions in scar-prone patients.

Patients may rarely complain of itching, which may be due to release of histamine like substance from P. acnes.



GRADING OF ACNE

There are various methods for grading severity of acne: **Simple grading by Indian authors:**[19]

Grade 1 : Mainly comedones, occasional papules

Grade 2 : Comedones, many papules, few pustules.

Grade 3: Predominantly pustules, nodules, abscesses

Grade 4: Mainly cysts or abscesses, widespread scarring

IAA (Indian Acne Alliance)grading of acne

Mild Acne (Grade 1) Predominance of comedones	Comedones<30 Papules < 10 No scarring
Moderate Acne (Grade 2) Predominance of papules	Comedones any number Papules> 10 Nodules< 3 Scarring +/-
Severe Acne (Grade 3) Many Nodules	Comedones any number Papules any number Nodules/Cyst >3 Scarring +

GLOBAL ACNE GRADING SYSTEM[20]

LOCATION	FACTOR
Forehead	2
Right cheek	2
Left cheek	2
Nose	1
Chin	1
Chest & upper back	3

No lesions- 0

Comedones-1

Papule -2

Pustule- 3

Nodules-4

Local score = Factor X grade (0-4)

GLOBAL SCORE is sum of local scores.

1 - 18 – mild

19 - 30 – moderate

31-38 - severe

>39 - very severe

MECHANISM OF ACNE SCAR FORMATION

Scarring in acne occurs due to abnormal healing process that occurs after the damage caused due to inflammatory process during the course of disease. These inflammatory events are brought about by cell mediated immune response. Scarring in acne is determined by severity of inflammation as measured by depth and duration.

However, strangely scarring doesn't occur in all patients of acne. Studies have found difference in infiltrate in the lesions of patients who develop scarring & those who do not[21] . In lesions from acne patients who were vulnerable to scar, a predominantly adaptive immune response was present, which was persistent and up-regulated in resolving lesions. The number of CD4 T cells was approximately half of those found in lesions of non-scarrers, but a high percentage of these cells were skin homing memory/effector cells, suggesting that these patients were sensitized to the causative antigens.

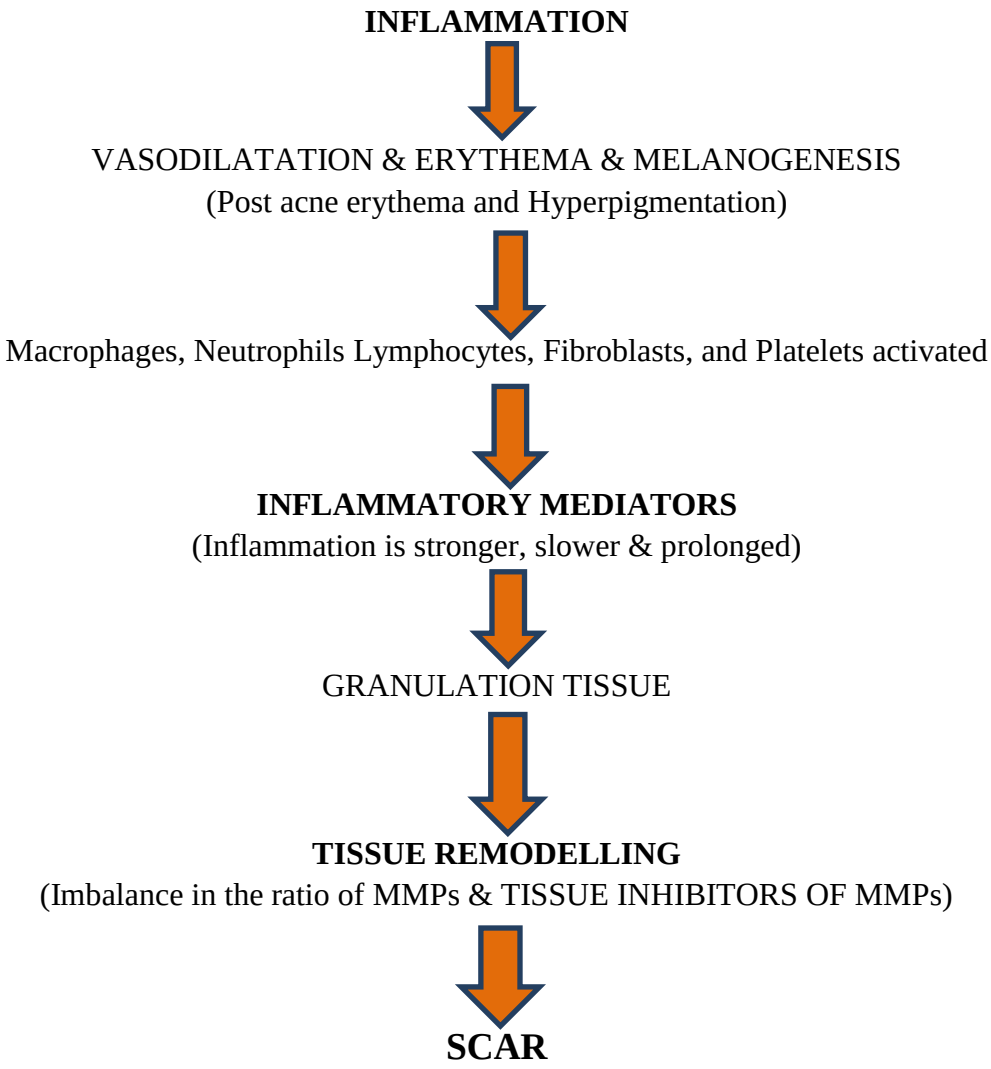
In developing lesions, although the numbers of macrophages, blood vessels and vascular adhesion molecules were high and similar to those present in lesions of non-scarrers, the numbers of langerhans' cells and the level of cellular activation were low, and comparable to levels found in normal skin, indicative of an ineffective response. However, in

resolving lesions, there was an up-regulation of the response with greater cellular activation and a further influx of macrophages and skin homing memory/effector cells. Certainly, the strong macrophage presence represents a dominant force in this response.

Keloidal scar occur on dark skin and is mapped to chromosome 2q23 and p11[22]. Damage to epidermis resulting in erythema and pigmentation is reversible, while damage to dermis resulting in atrophic scars is partially reversible and is irreversible in hypertrophic scars. Remodelling of collagen, the final step in tissue repair, is mediated by Matrix Metalloproteinases (MMP 1,2,9 and others) that cause the damage, and Tissue Inhibitors of Metalloproteinases (TIMP 1, 2, 3 mainly) which reduce the damage[21-28]. Alteration of ratio of MMPs/TIMPs, when is minimal atrophic scar occurs, when the ratio is more hypertrophic scar occurs.

In acne patients not prone to scarring, the time course was typical of a type IV delayed hypersensitivity response. In developing lesions there was significant angiogenesis and vascular adhesion molecule expression, with a large influx of activated CD4 T cells, macrophages (CD68) and Langerhans' cells (CD1a)[29]. Cell recruitment peaked at 48 hours after which there was a decrease in leukocytes, cellular

activation and a return to normal levels of blood vessels and vascular adhesion molecules in resolving lesions. Of the CD4 T cells, 50% were skin homing memory effector cells (CD45RO, CLA) and naïve cells (CD45RA) cells, whilst the remainder were unclassified (CD45RO−,CD45RA−, CLA−) which suggests that effective resolution occurred by both non-specific / innate and adaptive immune mechanisms[30] .



Types of acne scars[31]

- **Atrophic** – Icepick, Boxcar, Rolling, Macular atrophic, Perifollicular elastolysis.
- **Hypertrophic** – Keloidal, Papular, Perifollicular fibrosis
- **Mixed**
- **Unclassified**

Around eighty to ninety percent patients have atrophic scars. Only few have hypertrophic scars.

Goodman and Baron Classification of acne scars[32]

Grade 1: Macular - Erythematous, hyperpigmented, or hypopigmented marks

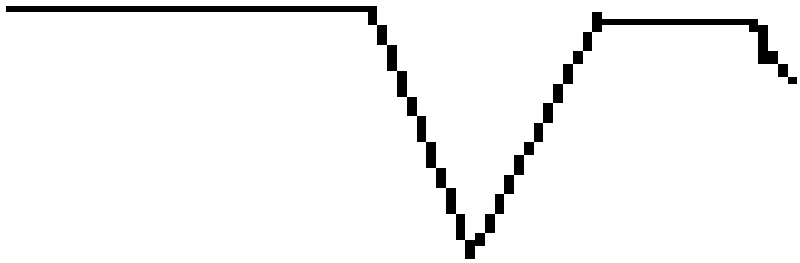
Grade 2: Mild Disease (Mild atrophy)

Grade 3: Moderate Disease (Moderate scarring)

Grade 4: Severe Disease - Scarring not flattened with manual stretching of the skin.

Morphological description of different types of acne scars

- **Ice-pick Scars** – They are jagged, deep, very narrow scars that extend into the dermis. They arise from comedones alone.



ICE PICK SCARS

- **Rolling scars**– These are shallow and wider than 4–5mm, and they appear as superficial shadowing and rolling or undulating appearance to the overlying skin

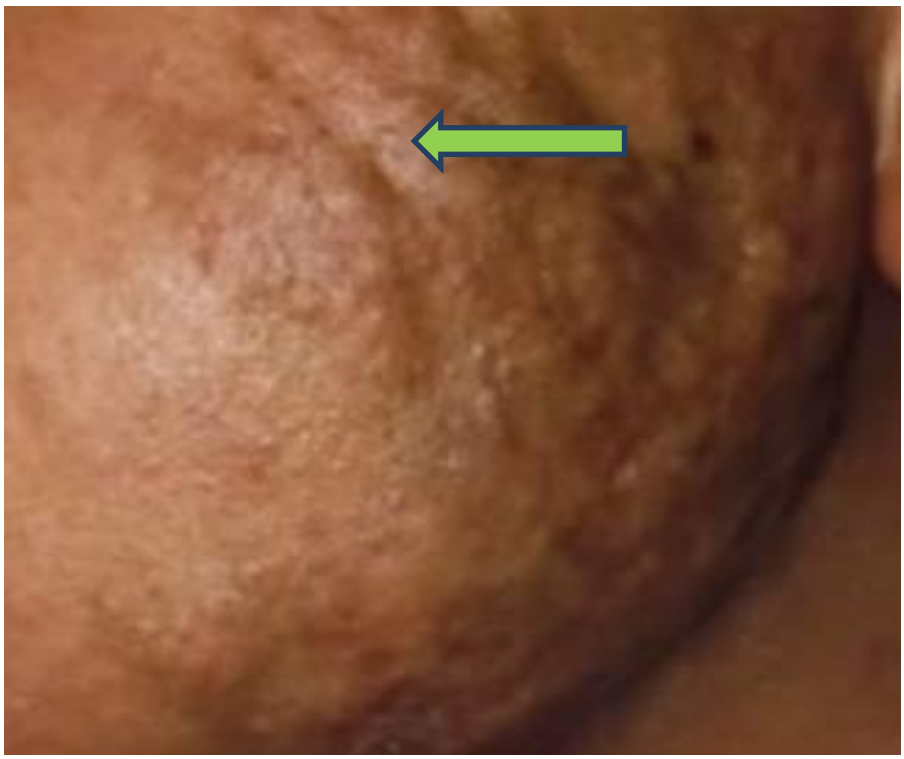
ROLLING SCARS

- **Boxcar scars**- A round or oval depressions with steep vertical sides.

BOX CAR SCARS

- **Perifollicular electrolysis** (PFE) is commonly found on the trunk which are multiple, follicular and atrophic.
- **Keloidal** scars extend beyond the sites of original inflammation and are most prevalent on the trunk.
- **Hypertrophic scars** do not extend beyond the extent of the original inflammation.

HYPERTROPHIC SCARS



Psychosocial effects of Acne and Acne scars

Patients with moderate to severe acne experience anxiety, shame, lack of self confidence, embarrassment, stress and impaired social contact. They mayalso face problem of unemployment. There have been reports of acne patients committing suicide[33] .

However it has to be noted that the psychological impairment is not always correlated with the severity of lesions. Acne lesions may settle down but its sequelae in form of acne scars in some subjects continue to affect their social and emotional well being. Television commercials and media further add to their emotional crisis by linking social success with cosmetically acceptable lesions. Severalsimple questionnaires have been developed to better understand the impact of acne in inducing anxiety, depression and impaired quality of life.

Scarring is also one of the poor prognostic factors in Acne[34] .Many patients continue to get new and severe lesions, making the treatment of scarring difficult. Other poor prognostic factors include:

1) Family History

2) Early onset: Mild facial comedones. Early and more severe sebum production, early onset relative to menarche.

3) Hyperseborrhoea

4) Site of acne: Truncal

5) Persistent

Although the diagnosis of acne is quiet simple. But following differentials must be kept in mind while making the diagnosis as early diagnosis and prevention of long term sequelae is important.

1) **Rosacea**- Occurs in older patients, absence of comedones, nodules, cysts and scarring. There may be facial flushing and specific triggers likeheat, spicy food, alcohol.

2) **Perioral dermatitis**- Lesions are itchy. Dry skin and absence of comedones. There is sparing of the vermillion border.

3) **Milia**- May cause confusion with white heads.They are commonly seen over infra-orbital region.

4) **Oil acne**: Hyperpigmented monomorphic papules, more common over extremities and trunk.

5) **Lupus miliaris disseminates faciei** – There is involvement of upper eyelid, upper lip.

6) **Drug induced acne**- History of drug intake. More widespread. The lesions are monomorphic.

7) **Sycosis barbae** – Mainly distributed over beard area. It is pruritic.Lesion are mainly pustular.

8) **Demodex Folliculitis**- It will be pruritic, absence of comedones, demonstration of mites.

9) **Sebaceous hyperplasia**- Appears as yellowish papules.There is absence of comedones

10) **Angio fibromas**- Skin colored papules mainly over nasolabial folds. Monomorphic lesions present.

11) **Warts**- Flat skin colored to hyperpigmented papules. Koebnerization can be seen.

Acne scarring can mimic scarring due to other underlying conditions like:

1) Hydroa vacciniforme

2) Ulerythema ophyrogenes

3) Acne keloidalis

4) Varioliform atrophy

5) Porphyria cutanea tarda

Various Syndromes associated with Acne

1) HAIR-AN Syndrome

- Hyper Androgenism
- Insulin Resistance
- Acanthosis Nigricans

2) **Apert syndrome** -

- Also known as Acrocephalosyndactyly.
- There is abnormal sensitivity to normal circulating levels of androgens.
- Craniosynostosis and early epiphyseal closure resulting in deformities of skull, hands and feet.
- Severe pustular acne along with other features like seborrhoea, hyperhidrosis, dystrophy of nails.

3) PAPA Syndrome

- Pyogenic Arthritis
- Pyoderma gangrenosum
- Acne

4) SAPHO Syndrome

- Synovitis
- Acne
- Pustulosis
- Hyperostosis
- Osteitis

5) Stein Leventhal syndrome

- It is also known as PCOD (Poly Cystic Ovarian Disease).
- Elevated levels of androgen with absent or infrequent ovulation.
- Acne, infertility, hyperinsulinemia

6) APAAN Syndrome

- Acne
- Patterned Alopecia
- Acanthosis Nigricans

VARIANTS OF ACNE

1) Neonatal acne -Settle spontaneously and leave little in the way of scars.

2) Neonatal Cephalic Pustulosis (NCP) – Presents in first 3 weeks of life, characterised by erythematous papular, pustular lesions on cheeks, chin, eyelids, neck, upper chest. No comedones seen. Role of Malassezia sympodialis and globosa implicated.

3) Infantile acne - Present later at 3- 6 months of age. Inflammatory papules can occur and may result in scarring.

4) Acne excoriee – In females usually those who keep picking the lesions repeatedly.

5) Senile acne–As a part of Dermatoheliosis i.e. Favre Racouchot Syndrome.

6) Drug induced- Various drugs can cause acneiform eruption like steroids, phenytoin, oral contraceptives.

7) Chloracne – Occupational acne caused by exposure to chlorinated aromatic hydrocarbons. Multiple comedones usually located on both sides of head and neck.

8) Mechanical acne – acne occurring at the site of physical trauma due to repeated mechanical or frictional obstruction of the pilosebaceous outlet.

9) Mallorca acne – Acne lesions specially over upper trunk after holiday in a hot, humid environment

10) Tropical acne- Also known as hydration acne .In those who work in hot humid environment.

11) Acne tarda–Acne in adults. Usually acne subside in early twenties, but in some continues in adult life.

12) Pomade acne – Pomades are greasy preparations used to defrizz curly hair. Lesions commonly over the forehead.

13) Acne conglobate – It's a severe form of acne. Mulitple inflammatory papules, tender nodules and abscesses commonly

coalescing to form draining sinuses. It is a difficult to treat condition.

14) Acne fulminans – Acne associated with systemic features like fever, polyarthropathy, marked leucocytosis, weight loss, anorexia and general malaise.

15) Pyoderma faciale – Also known as Rosacea Fulminans. Seen commonly in context of emotional stress, with sudden eruption of many inflammatory pustules and nodules, predominantly over face. The lesions are preceded by episode of flushing.

16) Gram- negative folliculitis – It can occur as a complication of long term oral or topical antibiotic therapy to treat acne. Klebsiella, Escherichia coli, Serratia marescens, Proteus mirabilis or Pseudomonas aeruginosa are implicated.

17) Detergent acne – Seen in those who wash their face many times aday. Trauma and alkalinity of soap may be responsible for aggravation of lesions.

COMPLICATIONS OF ACNE

- Scarring
- Hyperpigmentation
- Depression, suicidal ideation, anxiety[35] .
- Psychosomatic symptoms(pain , discomfort)
- Embarrassment
- Body dysmorphic disorder
- Social inhibition.
- Unemployment[36] .

TREATMENT OF ACNE

Because prevention is better than cure, proper and early treatment of acne is the first step in the ladder of treatment of acne scars. The aim of management is to relieve symptoms, limit disease activity so as to prevent new lesions and scarring and negative impact on the quality of life.

VARIOUS MODALITIES FOR TREATING ACNE SCARS CAN BE GROUPED AS :

1) Topical therapy

- Topical antibiotics like Clindamycin, erythromycin- Usually in combination with benzoyl peroxide.

- Benzoyl peroxide – It is a strong antimicrobial. Resistance to it has not been reported. Microsponge delivery system helps in controlled and targeted delivery of the drug molecule and also reduces the irritancy.

- Azelaic acid – Dicarboxylic acid with antimicrobial and comedolytic property. Also helps in decreasing post acne pigmentation.

- Topical retinoids – They are comedolytic, anti- inflammatory as well as inhibit P. acnes.

- Dapsone, Nicotinic acid

2) **Oral therapy** –

- Tetracyclines – They are commonly used. They cause a decrease in free fatty acids present in sebum, act against P. acnes and are anti-inflammatory.

- Macrolides – Erythromycin and Azithromycin are used.

➢ Retinoids–Isotretinoin use has revolutionized the anti-acne therapy.

Mechanism of action of retinoids:

- Decreases seborrhoea
- Comedolytic
- Inhibits P. acnes
- Anti- inflammatory

➢ Others - Trimethoprim-sulphamethoxazole, Clindamycin, Dapsone

3) **Hormonal therapy**- Oral contraceptives, Antiandrogens, Gonadotropin releasing hormone agonists.

4) **Physical modalities**-

➢ Phototherapy – UV light, Photodynamic Therapy

➢ Lasers – Pulsed potassium titanyl phosphate laser (532 nm)1320 nm Nd- YAG Laser,1540 Erbium glass laser.

5) Newer therapies –

- Green Tea- Anti-inflammatory and interferes with IGF-1 signalling thereby reducing sebum production.

GLOBAL ALLIANCE ALGORITHM FOR IMPROVING OUTCOME IN ACNE[37]

	MILD		MODERATE		SEVERE
	COMEDONAL	**PAPULAR/PUSTULAR**	**PAPULAR/PUSTULAR**	**NODULAR**	**NODULAR/CONGLOBATE**
1st choice	Topical retinoid	Topical retinoid + topical antimicrobial	Oral antibiotic + topical retinoid +/- BPO	Oral antibiotic + topical retinoid +/- BPO	Oral Isotretinoin
Alternatives	Alt. topical retinoid or azelaic acid or salicylic acid	Alt. topical antimicrobial + alt. topical retinoid	Alt. oral antibiotic + alt. topical retinoid +/- BPO	Oral isotretinoin or alt. oral antibiotic + alternate topical retinoid+/- BPO / Azelaic acid	High dose oral antibiotic+topical retinoid + BPO
Alternatives for females	See 1st choice	See 1st choice	Oral antiandrogen + topical retinoid + /azelaic acid +/- topical antimicrobial	Oral antiandrogen + topical retinoid +/- oral antibiotic +/- alt. anti microbial	High dose oral antiandrogen + topical retinoid +/- topical antimicrobial
Maintenance therapy	Topical retinoid	Topical retinoid+/- BPO			

Various procedures used for acne scars are :

1) Chemical peels/ CROSS (chemical reconstruction of skin scars)

2) Subcision

3) Dermabrasion

4) Microdermabrasion

5) Laser resurfacing

6) Punch elevation and excision

7) Skin needling

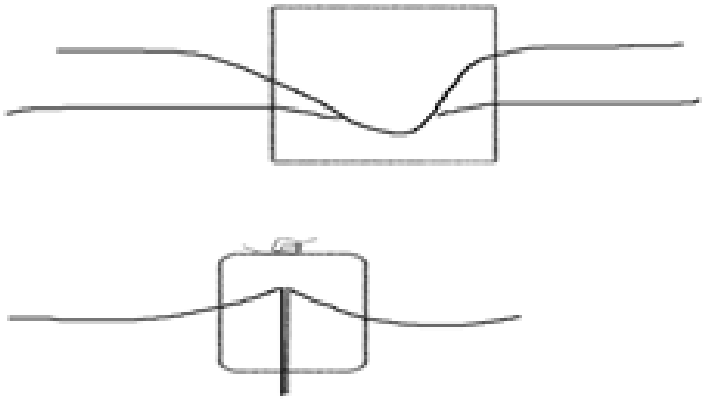
8) PRP

9) Fillers

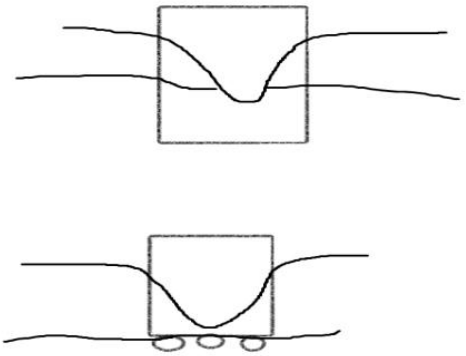
Scar excision

Tiny/minute, well defined scars can be removed by punch excision, elevation, subscision.

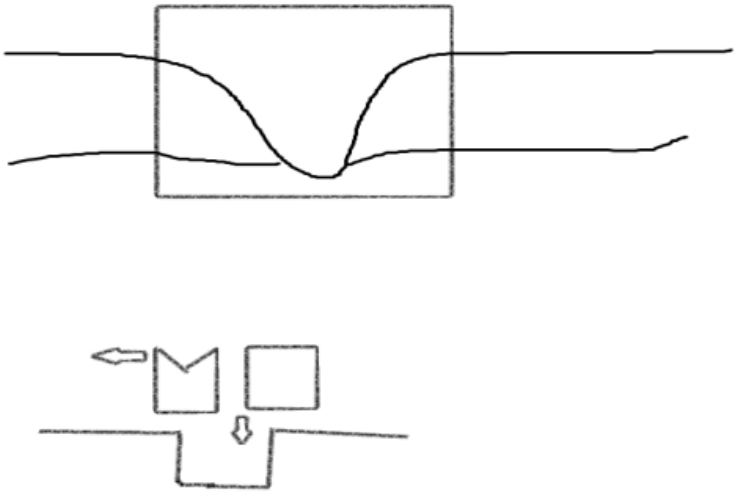
- **Punch excision** - The scar is excised with a punch and the skin is sutured together



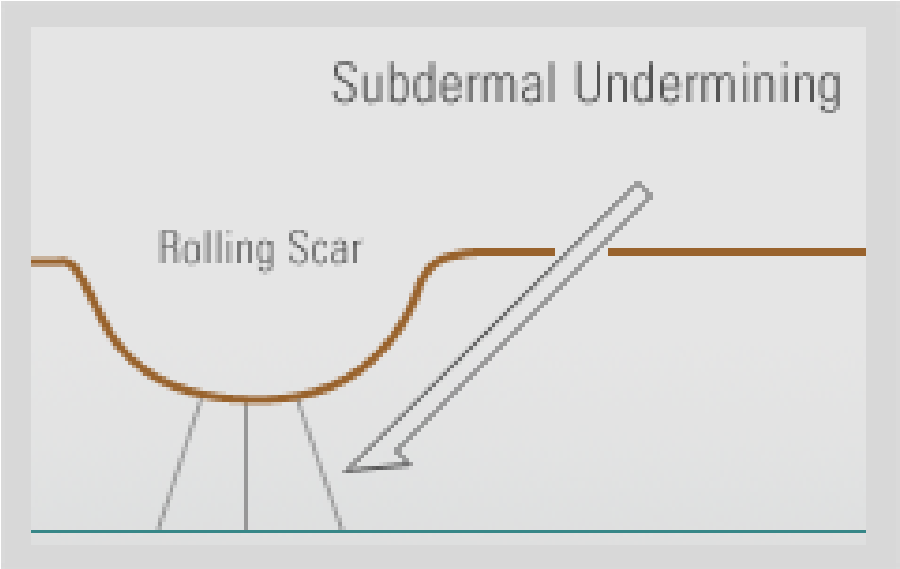
- **Punch elevation -** Punch of appropriate size is inserted in to the scar till base and adhesions at sides are cut, the plug is then raised. This procedure is called punch elevation



- **Punch excision and grafting**-Scars are removed with a punch and is replaced by donor graft from retroauricular area



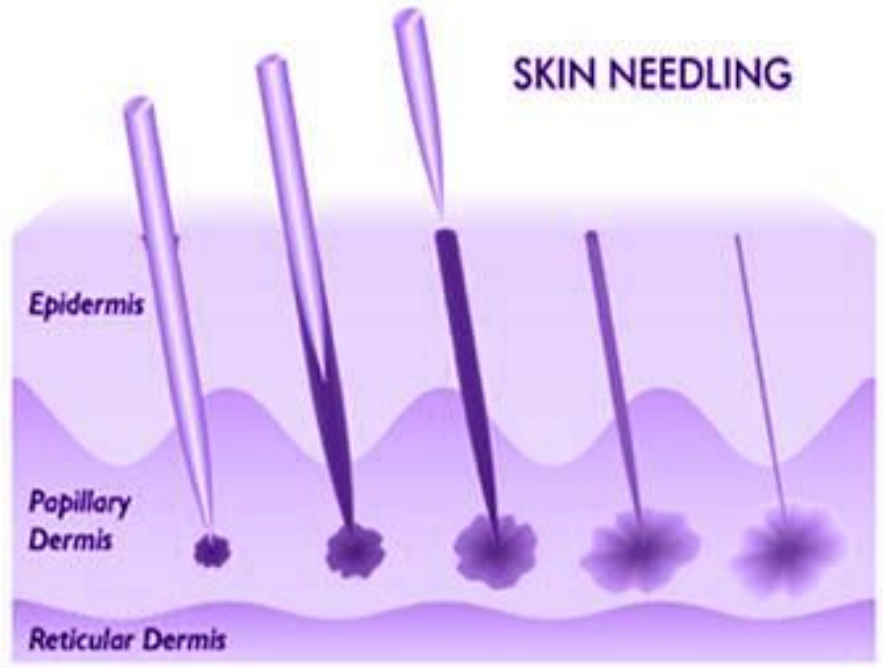
- **Subcision** - Surgically freeing up the deeper layers of the skin so the scars are no longer bound down. A needle or surgical scissors are used to physically separate the dermis and subcutaneous tissue.



- **Microdermabrasion** – Skin resurfacing with Aluminium oxide or sodium chloride microcrystals to superficially remove stratum corneum and epidermis.

- **Dermabrasion**: Involves the controlled deeper abrasion of the upper tomid layers of the skin with a strong abrasive devices including a wire brush, diamond wheel or fraise, sterilized sand paper, salt crystals, or other mechanical means.

- **Microneedling**: Involves repeatedly puncturing the skin with tiny, sterile needles (microneedling the skin) in order to induce endogenous production of cutaneous collagen.



- **Chemical peeling** – Exfoliation of skin induced by the use of chemical cauterant or escharotics agent on the skin

Peels used commonly

- TCA
- Alpha hydroxyl acids -glycolic acid
- Salicylic acid
- Retinoic acid
- Jessner's solution
- Phenol
- 5 – Fluorouracil
- Alpha keto acid

Types of Chemical peels

- ❖ Very superficial- glycolic acid 10 to 30%, TCA 10%, Jessner's solution
- ❖ Superficial- glycolic 50 to 70%,TCA 10 to 35%

- Medium depth – glycolic >70%, TCA 35 to 50%
- Deep – phenol 88%

TCA CROSS –focal application of higher concentrations of trichloroacetic acid (TCA) and is pressed hard on the entire depressed area of atrophic acne scars. This technique is called chemical reconstruction of skin scars (CROSS)

Laser – CO2 Laser is used which has a wavelength of 10600 nm.Resurfacing of acne scars done by sculpturing the edges.

Fillers- Purified bovine collagen is injected in the defective areas.

Now degradable, synthetic implants like hyaluronic acid are used, to avoid risks of sensitizations & foreign body reaction.

Freeze dried, radiation treated fascia lata from human cadaver implant is placed at site of each scar by creating an intradermal pocket at site with help a needle. Alternate method is autologus fat transplantation to acne scars.

Most of the procedures mentioned above have been used over years for the treatment of acne scars. However most of them have one or more drawbacks like :

- Risk of hyperpigmentation
- Keloid formation
- Cost factor
- Some procedures have long downtime.

There is a need to find simpler, safer and effective means to add to this list of procedures which can be used either alone or in combination with the above methods to provide satisfactory results to the patients.

PLATELET RICH PLASMA

COMPONENTS OF BLOOD:

Blood consists of Red blood cells, White blood cells, Platelets and Plasma.

Plasma:

- Relatively clear, yellow tinted
- Constitutes 55% of the blood volume.
- Carries RBCs, WBCs and platelets.
- Contains various hormones, enzymes, proteins and antibodies.

Red Blood Cells:

- Large microscopic cells without nuclei.
- They normally make 40- 50% of total blood volume.
- Main role is oxygenation of tissues.

White Blood Cells:

- Constitute 1% of total blood volume
- Component of body's defence mechanism.
- Neutrophils, eosinophils, basophils, monocytes, lymphocytes.

Platelets:

- Cytoplasmic fragments of megakaryocytes (a type of white blood cell), which are produced in the bone marrow.
- Round or oval inshape, approximately 2 mm in diameter.
- Platelets do not have nuclei but contain organelles and structures such as mitochondria, microtubules, and granules (α, δ, λ).

The α granules contain around 30 bioactive proteins which play a role in hemostasis and tissue healing.

In PRP therapy the basic objective is applying supra-pharmacological dose of platelets directly at the site where tissue regeneration is required.

PRP therapy is being used in other medical fields but it is new in dermatology.

It helps to rejuvenate & regenerate injured tissues and also modulates wound healing.

DEFINITION OF PRP

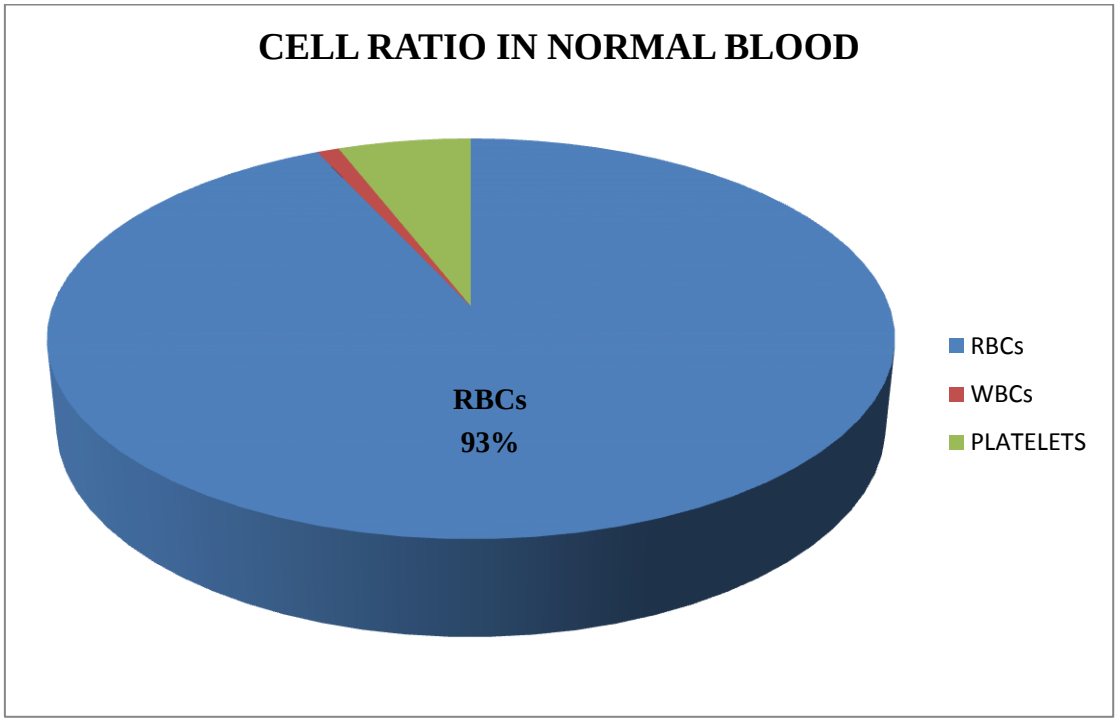
Platelet-rich plasma (PRP), also called as autologous platelet gel or plasma-rich growth factors and platelet-concentrated plasma means "abundant platelets that are concentrated into a small volume of plasma."[38]

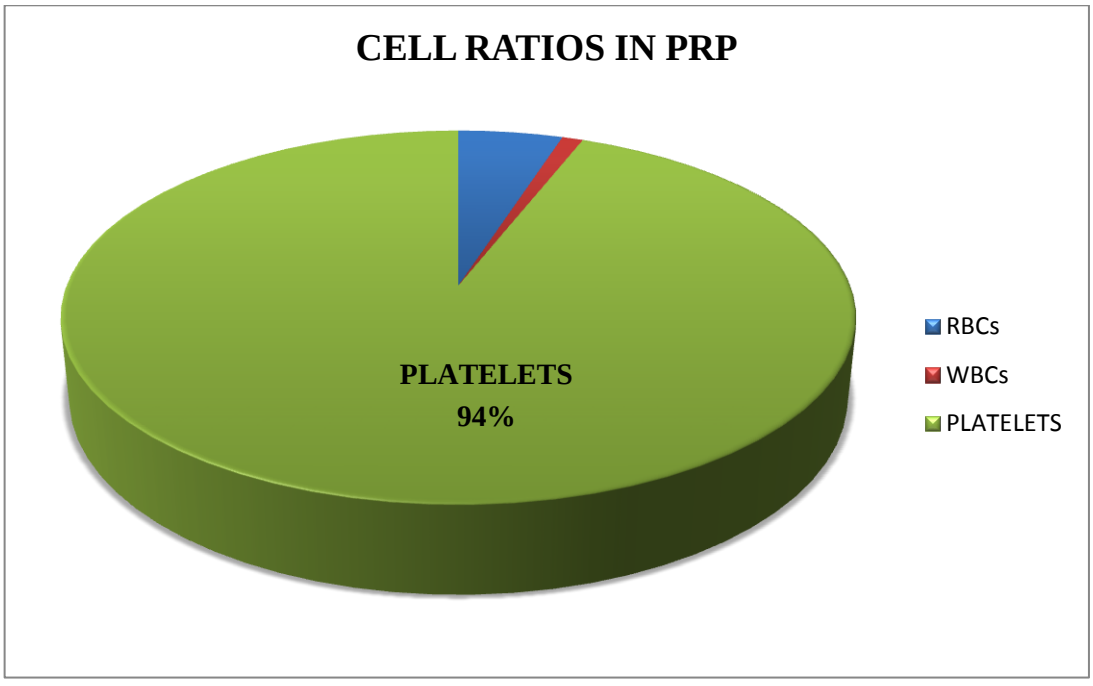
The discovery of platelet-derived growth factor (PDGF) in promoting wound healing, angiogenesis and tissue remodelling threw light on this novel autologous therapeutic modality. This mixtures of GFs plays pivotal role in modulation of tissue repair and regeneration[39] .

Degranulation of the pre-packaged GFs in platelets occurs upon "activation" i.e.on coming in contact with coagulation triggers.

The secreted GFs in turn bind to their respective transmembrane receptors expressed over adult mesenchymal stem cells, osteoblasts, fibroblasts, endothelial cells, and epidermal cells.

This further induces an internal signal-transduction pathway, unlocking the expression of a normal gene sequence of a cell like cellular proliferation, matrix formation, osteoid production, collagen synthesis, etc., thereby augmenting the natural wound-healing process.


CELL RATIO IN NORMAL BLOOD
RBCs
93%
RBCs
WBCs
PLATELETS


CELL RATIOS IN PRP
PLATELETS
94%
RBCs
WBCs
PLATELETS

HISTORY OF PRP

PRP has been therapeutically used to accelerate woundhealing and tissue repair in dentistry since 1998, and theclinical application of PRP was recently expanded to other fields, including cardiac surgery, ophthalmology, oral and maxillofacial surgery, orthopedic surgery, plastic surgery, sports medicine, and cosmetic medicine.[40]Different ways of preparing PRP have come into existence : from conventional blood centrifugationto commercial systems; activated by adding collagen, calcium and/or thrombin, by glass contact orby freezing cycles; applied as platelet suspension or as agel; and the methodology still continues to broaden.

It is a biological product which is being prepared using different protocols. The injection of platelet-derived factor into a tissue appears to trigger the ound healing process without any actual wounding. It is believed that PRP induces local tissue re –modelling and angiogenesis by activating tissue-resident progenitor/stem cells and may also recruit bone-marrow-derived progenitor/stemcells.

For preparing PRP , two methods have been explained depending upon the number of centrifugation steps used: one is the single spin method and the other is double spin method. Double spin method has

been shown to be better yielding than the single spin method[41] .The first centrifugation is slow to avoid spinning down platelets, whereas the second spin is fast, so the platelets are spun down and can be collected easily for various therapeutic indications.

After preparation, platelet-rich plasma is stable, in the anti-coagulated state, for 8 hours[42] .The platelet-rich plasma must be activated for the platelets to release their alpha granule content.

PRP is prepared in a day care setting just prior to the procedure. The process must be carried out under strict aseptic conditions as well as optimum temperature regulations i.e.20-22°C. In order to inhibit platelet aggregation, it is prepared with an anticoagulant, commonly using anticoagulant citrate dextrose solution formula A (ACD-A) [43] or sodium citrate. The platelets need to be sequestered in high concentrations, enough for achieving therapeutic benefit and in a viable state at the same time, so that they can actively secrete their GFs.

So this modern technology allows us to concentrate platelets and white blood cells from a patient’s blood and to induce the release of growth factors by injecting the solution directly into injured tissue, stimulating the same healing process but in a more directed form.

Various growth factors present in PRP are –

1) **Transforming growth factor beta (TGF) β1** – mediates angiogenesis.**TGFβ 2**- Acts as chemotactic for fibroblasts, keratinocytes and macrophages. It is also mitogenic for smooth muscle cells and fibroblasts. It also has potential to regulate matrix proteins, collagen and proteoglycans.

2) **Platelet derived growth factor (PDGF) αα** –It is chemotactic for fibroblasts and macrophages. PDGF ββ and αβ – They are mitogenic for fibroblasts, smooth muscle cells and endothelial cells.

3) **Vascular Endothelial Growth Factor (VEGF)-** Chemotactic and mitogenic for endothelial cells.

4) **Epidermal growth factor** – It is mitogenic for fibroblasts, keratinocytes and endothelial cells.

5) **Fibroblast growth factor-2 (FGF-2)-** It has a role in tissue organization and regeneration.

6) **Fibroblast growth factor 9-** Helps in regeneration of hair follicle.

7) **Hepatocyte growth factor** – Helps in regeneration.

PRP PREPARATION BY MANUAL DOUBLE SPIN METHOD[44]

According to The American Association of Blood Banks technical manual, first the ‘platelet-rich plasma’ is separated from whole blood by ‘soft or light-spin’ centrifugation and subsequently the platelets are concentrated by ‘ hard or heavy-spin’ centrifugation . After which the supernatant plasma is removed. The basic principle behind the PRP separation procedure is as follows: Different blood components have different specific gravities. So on centrifugation they get separated into different layers.

As the Red blood cells are heaviest they settle at the bottom, followed by white blood cells and the top layer is of platelets as they are lightest. In the first step aim is to separate the plasma from rest of the components. This is done by a slow centrifuge, after which platelets get concentrated just above the buffy coat. In the later step, centrifugation is faster so that platelets get concentrated and settle down at the bottom of the test tube.

Approximately 3/4 of the supernatant is discarded and the platelet-rich pellet is re-suspended in remaining amount of plasma. Calcium

chloride (CaCl2) or thrombin is then added as an “activator” to activate the platelets and hence degranulation of GFs to yield “activated PRP”.

Maximum secretion of the growth factors occur within ten minutes of activation, so the activated PRP must be used as early as possible.

There is variability in the yield of platelets obtained depending upon the methods used, rate and time of spin, anticoagulant used and even the size and shape of container. The platelet yields may vary from 4 to 7 times the baseline. To assure the viability of platelets the temperature should be maintained between 20- 22 degree centigrade. Trypan blue staining can be used to confirm the viability.

Double spin method is used preferably over single spin method, as studies have shown that the single spin method failed to achieve the therapeutic levels of platelet .As there are different protocols, devices and centrifuge speeds for preparing PRP, so different types of platelet concentrates are obtained. It was Ehrenfest et al who first proposed a classification for the platelet concentrate[45] .

He classified them into four types depending upon the leucocyte and fibrin content:

1) **P-PRP (Pure Platelet Rich Plasma)** - This can be prepared by collecting only the buffy coat alone after the first soft spin. Very few leucocytes will be present.

2) **L-PRP(Leucocyte and Platelet Rich Plasma)** – This type contains mostly platelets with few but appreciable amount of leucocytes. There is difference in collection of PRP. After soft spin, plasma, buffy coat and topmost layer of RBC is harvested. Later after hard spin lowest fraction of product is harvested which contains all platelets and few leucocytes.

3) **P-PRF (Pure Platelet Rich Fibrin)** –This is obtained by mixing PRP with activator and incubating it for some time so that a stable platelet rich fibrin clot is formed .

4) **L-PRF (Leucocyte and Platelet Rich Fibrin)** – In this no anticoagulant added and no activator required. First blood is collected without any anticoagulant and centrifuged without delay. The process results in three layers. L-PRF layer is formed in middle and harvested.

CONCENTRATION OF PLATELETS IN PRP

The average concentration of platelets in blood is 200,000 ± 75,000/μL. For a preparation to be labelled as PLATELET RICH, the concentration of platelets should rise to level of five to ten times the base line[46] .

Now a days in market, various automated devices are available for preparing PRP. However these devices are expensive than manual methods and the commercial interest of the manufacturers can deteriorate the quality of platelet concentrates.

INDICATIONS OF PRP IN DERMATOLOGY

1) **Androgenetic Alopecia**–PRP has been used as incubation medium in Follicular Unit Transplant as well as Mesotherapy[47]-[48] .

2) **Alopecia areata** – Significant hair growth has been seen in other alopecias like alopecia areata and telogen effluvium [49] .

3) **Skin rejuvenation** – PRP has become very popular in asthetic medicine. It is shown to remove photo damaged extra cellular matrix and induce synthesis of new collagen. PRP can be applied topically under occlusion or given as intradermal injections [50]-[55] .

4) **Acne scars and contour defects**–PRP has been used as mesotherapy alone or in combination with other modalities like dermaroller or laser resurfacing [56]-[60] .

5) **Wound ulcers and connective tissue disease associatedulcers**- Stasis ulcers, trophic ulcers, diabetic ulcers and traumatic ulcers have shown good healing after treatment with PRP [61]-[63] .

6) **Striae distensae**[64]-[65] - Kim et al used an intradermal radio-frequency device which delivered higher energy fluencies directly to the dermis, along with injecting PRP as a filler through its needle electrode.

7) **Lipodermatosclerosus**[66] – There is a single case report in which five sessions of PRP led to complete healing of venous ulcer and marked improvement in the pigmentation and induration.

8) **Lichen Sclerosus**[67] -PRP along with autologous fat transfer is a novel technique in management of lichen sclerosus of vulva.

SAFETY OF PRP

Autologous PRP is quite safe. The mitogenic effect of PRP is limited tothe normal healing process. PRP is not mutagenic as whatever growthfactors it delivers, act through signal transduction only[68] .These growth factors do not enter the cells or nucleus .There may be local injection site reactions like transient erythema or Pain. Secondary infection is rare when the procedure is carried out under strict septic precautions. Since PRP is autologous, there is no risk of transmission of Hepatitis B, C or HIV.

AIM AND OBJECTIVE OF THE STUDY

To assess efficacy and safety of PLATELET RICH PLASMA (PRP) for treatment of acne scars.

MATERIALS AND METHODS

Study design

- Type of study – Non randomized Prospective Interventional study

Study population

- Sample size – forty patients

Study period

- JUNE 2013 to MAY 2014

Place of study

- Department of Dermatology,

  Government Stanley Medical College & Hospital

  Chennai.

A brief and relevant medical history and physical examination (Annexure 1) was done at screening visit to ensure relevant eligibility criteria. Patients were elaborately explained about the procedure and consent was taken. Then the patient thoroughly evaluated and grading of acne scars (Goodman and Baron Classification of acne scars) done.

Patient were explained about PRP therapy, benefits of therapy, possible side effects and prognosis of treatment.

Informed consent was taken. Digital photographs of face taken.

Platelet-rich plasma was injected by multiple tiny punctures under the dermis, with or without topical local anesthesia. Up to 6 sittings were given within a 6-month time frame. Either the patient improved to grade 1 or a maximum of 6 sittings, whichever was earlier. These were performed 4 weeks apart. At the end of treatment duration, scars were graded using grading system as used in the beginning, photographs taken and compared.

PRE-TREATMENT CONSULTATION

- Patients were well informed about the procedure and the possible side effects.
- Informed and written consent were obtained
- Complete history regarding onset, duration, any other co-existing systemic illness, past history of any treatment for the same, Isotretinoin use, immunosuppressive agents, Hepatitis B co-infection were also noted.
- Proper Counselling of patient is very important.
- The motivation of the patient is assessed.

INCLUSION CRITERIA:

- Both sexes
- Age >18 years
- Atrophic Acne scars – rolling and boxcar scars
- Patient willing for follow up and to be photographed.

EXCLUSION CRITERIA:

- Active nodulocystic acne.
- Keloidal tendency.
- Bleeding disorder.
- Oral steroids.
- Anticoagulant therapy.
- Any active skin infection.
- Pregnancy
- Skin diseases like SLE, porphyrias
- Metabolic and systemic disorders.

- Patients who received Oral Isotretinoin for acne during last one month

PRE PROCEDURE WORK UP

- Hb, TC, DC, ESR, Platelet count
- Bleeding time, clotting time
- Fasting blood glucose
- Renal function test – blood urea, serum creatinine
- SGOT
- SGPT
- Screening for Hepatitis B, HIV, VDRL testing.
- Informed consent and photographs

GRADING OF ACNE SCARS

The grading of acne scars was done according to the following scale (Goodman and Baron Classification of acne scars)

GRADE 1- Macular-Erythematous, hyper- or hypopigmented flat marks. No problem of contour like other scar grades.

GRADE 2- Mild- Mild atrophic scars that may not be obvious at social distances of >/= 50 cm and may be covered adequately by makeup or the normal shadow of shaved beard hair in men.

GRADE 3- Moderate- Moderate atrophic scarring that is obvious at social distances >/= 50cm and is not covered easily by makeup or the normal shadow of shaved beard hair in men, but is still able to be flattened by manual stretching of the skin

GRADE 4-Severe-Severe atrophic scarring that is evident at social distances >50 cm and is not covered easily by makeup or the normal shadow of shaved beard hair in men and is not able to be flattened by manual stretching of the skin.

INSTRUMENTS AND MATERIALS REQUIRED

Centrifuge machine

Sterile test tubes

Sterile pipettes

Sterile bowls

Anticoagulant Acid citrate dextrose

10% calcium chloride as activator

Topical numbing cream

Insulin syringe

Sterile gauze

PRP PREPARATION

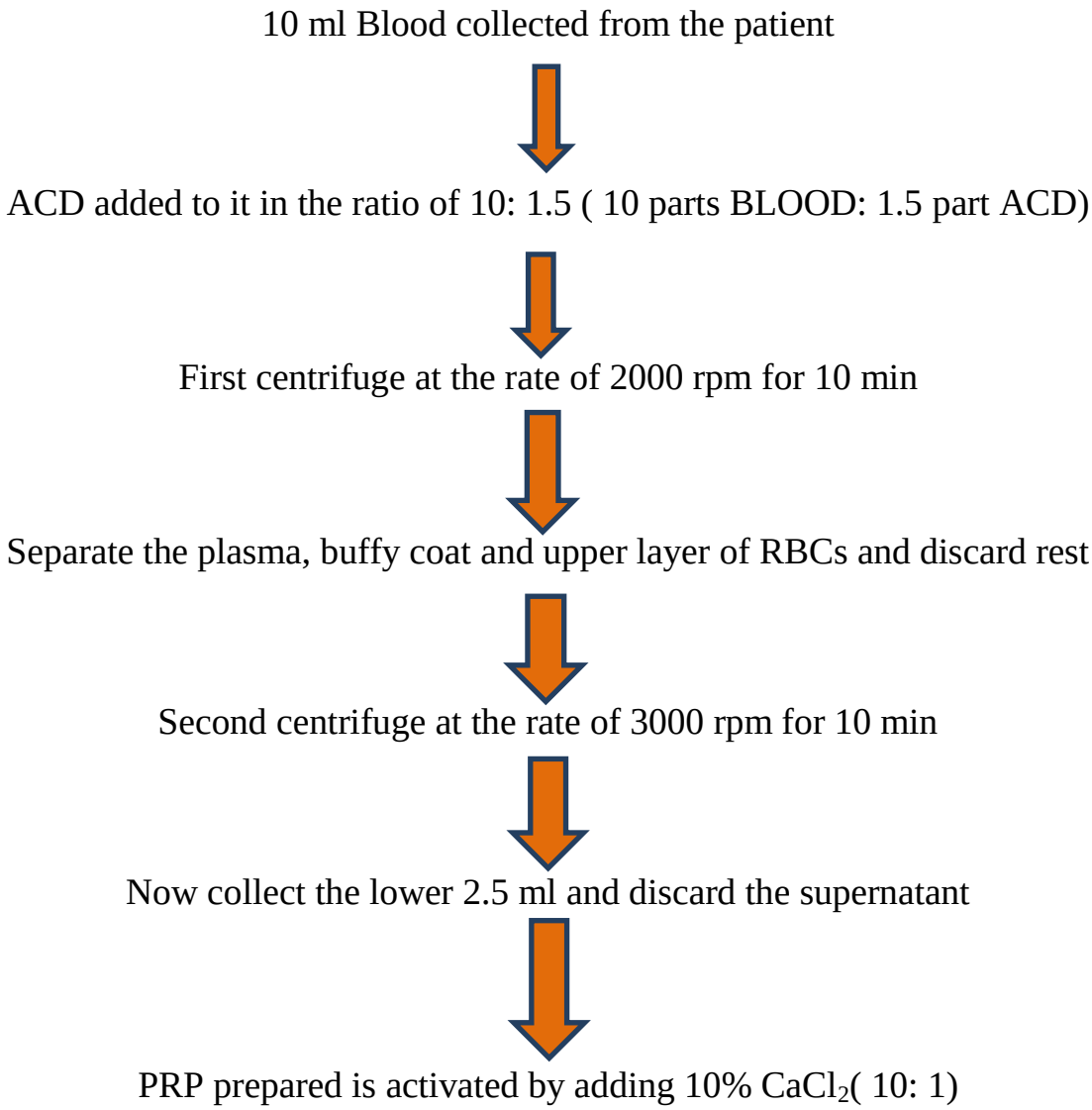
Full process is carried out under strict aseptic conditions. Room temperature maintained at 22- 26 degree centigrade.

10 ml blood is collected from the patient in the centrifuge test tubes (labelled with patient's name and age) and mixed with anticoagulant ACD (Acid Citrate dextrose) in the ratio of 10: 1.5 .

The tube is then placed for first centrifugation i.e. soft spin at the rpm of 2000 for ten minutes. At the end of this plasma gets separated and we pipette out plasma, buffy coat and uppermost layer of red blood cells into another tube. The uppermost layer of RBCs are collected because it has been shown that a portion of young platelets is present in this layer .

This collected part is again subjected to second centrifugation .This is hard spin at the rpm of 3000 for another ten minutes . At the end of this step, platelets settle down at the bottom of the test tube . The upper three-

fourth of supernatant is discarded without disturbing the lower layer and lowest portion obtained is the Platelet Rich Plasma. PRP is now ready for the use. It should be activated just before injection into skin by adding 10 % calcium chloride to it in the ratio of 1: 10 (1 part $CaCl_2$, 10 parts PRP) and agitating it by vigorous shaking.



PROCEDURE PROPER

- The area to be treated is anaesthetized with topical anasethesia like EMLA (Eutectic mixture of lidocaine and prilocaine).

- 10 ml of blood is drawn from the patient, which is used for preparation of Platelet Rich Plasma according to the procedure mentioned above and under strict aseptic precautions.

- After about 45 minutes the area to be treated is cleaned with spirit. Skin is stretched and the Activated PRP is loaded in insulin syringe and injected into the scars and around it through multiple punctures.

- Mild erythema can be seen immediately after the procedure. Face is wiped with a mild cleanser. Patient advised not to vigorously rub the face for 12 hours and not to take aspirin or other anti- inflammatory drugs while on therapy.

- No dressing is required. No other specific instruction.

- The same procedure is carried at interval of every 4 weeks for 6 months.

- At every visit clinical grading is done, patient satisfaction assessed and clinical photograph taken.

The procedure was continued until either the grading of scars became 1 or upto maximum of 6 sittings, whichever came first.

Patients' satisfaction was accounted at the end of the sittings according to following scale:

SCORE	PATIENT'S SATISFACTION
0	POOR
1	FAIR
2	GOOD
3	VERY GOOD
4	EXCELLENT

Dermatology Life Quotient Index(DLQI) was calculated before and after the completion of the treatment using the following questionnaire :

1. Over the last week, how itchy, sore, painful or stinging has your skin been?

2. Over the last week, how embarrassed or self conscious have you been because of your skin?

3. Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden?

4. Over the last week, how much has your skin influenced the clothes you wear?

5. Over the last week, how much has your skin affected any social or leisure activities?

6. Over the last week, how much has your skin made it difficult for you to do any sport?

7. Over the last week, has your skin prevented you from working or studying?

If "No", over the last week how much has your skin been a problem at work or studying?

8. Over the last week, how much has your skin created problems with your partner or any of your closefriends or relatives?

9. Over the last week, how much has your skin caused any sexual difficulties?

10. Over the last week, how much of a problem has the treatment for your skin been, for example, by making your home messy, or by taking up time?

DERMATOLOGY LIFE QUALITY INDEX was calculated as following before and after the treatment.

0-1 = no effect at all on patient's life

2-5 = small effect on patient's life

6-10 = moderate effect on patient's life

11-20 = very large effect on patient's life

21-31 = extremely large effect on patient's life.

OBSERVATIONS AND RESULTS

Study population

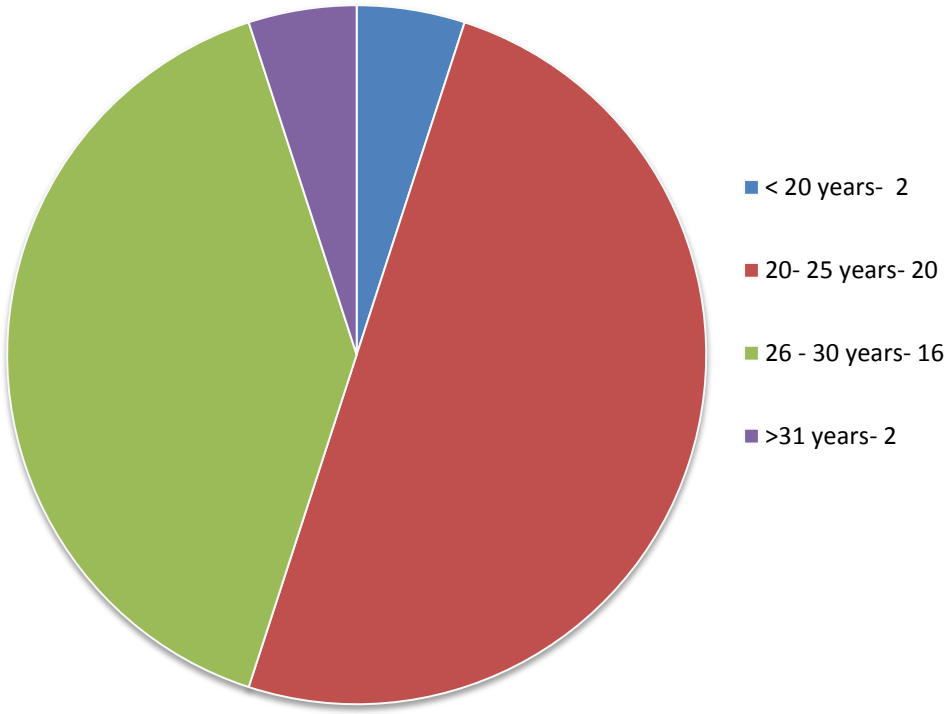
This study included total 40 patients 30 male and 10 female patients.

Youngest age is 18 years of age and oldest is 31 years of age. All fulfilled the inclusion and exclusion criteria

TABLE 1 – AGE WISE DISTRIBUTION OF STUDY POPULATION

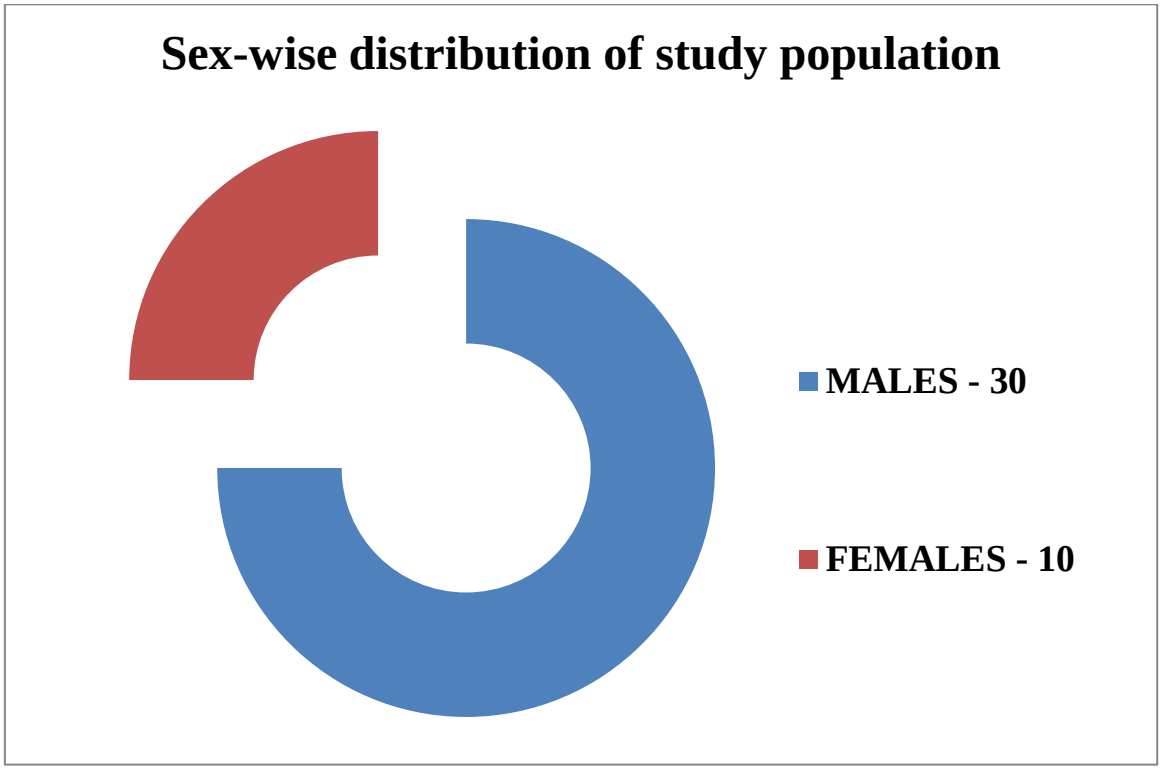
Age group	Number of patients
<20	2
20 to 25	20
26 to 30	16
>31	2

CHART NO. 1: AGE WISE DISTRIBUTION OF STUDY POPULATION



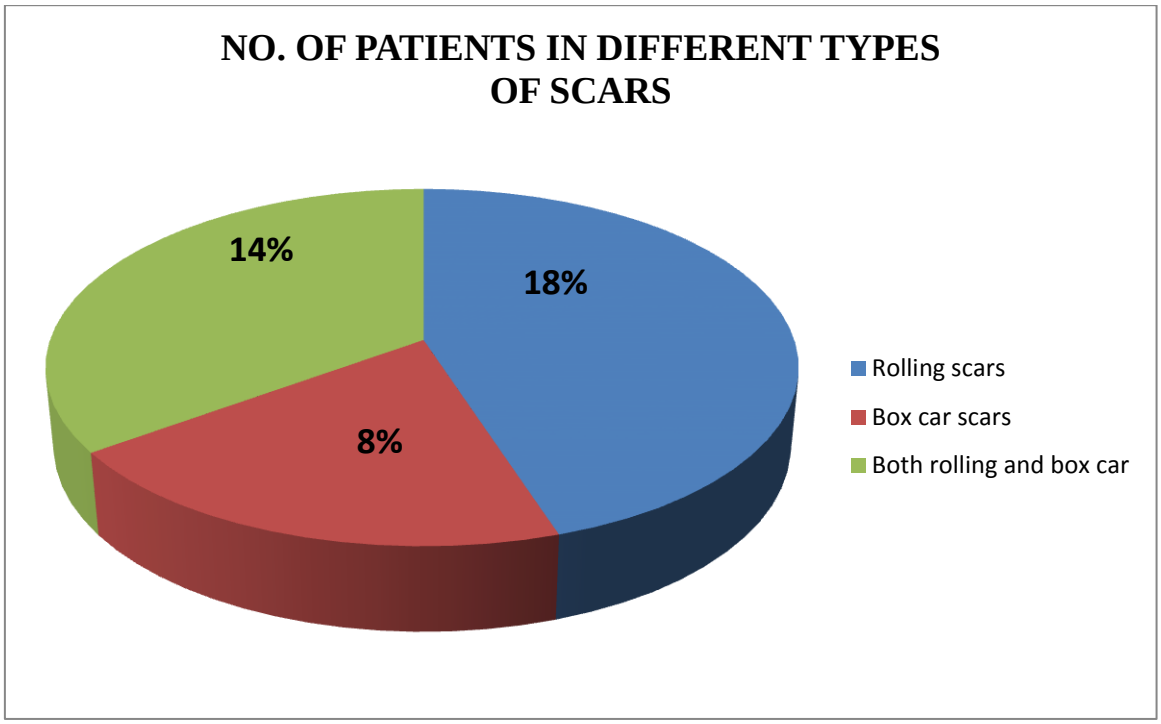
SEX WISE DISTRIBUTION OF STUDY POPULATION

Males	Females
30	10



TYPE OF ACNE SCARS INCLUDED IN THE STUDY

Type of scar	Number of patients
Rolling	18
Boxcar scar	8
Both boxcar and rolling	14



After 3 sittings of the procedure appreciable changes were seen on the skin surface of most of the patients.

At every visit, the treated area over patient's face was photographed and compared with the previous visit photograph and grading was done according to the scale mentioned above. In most of the cases the depth of scars was reduced making the scars less obvious than before.

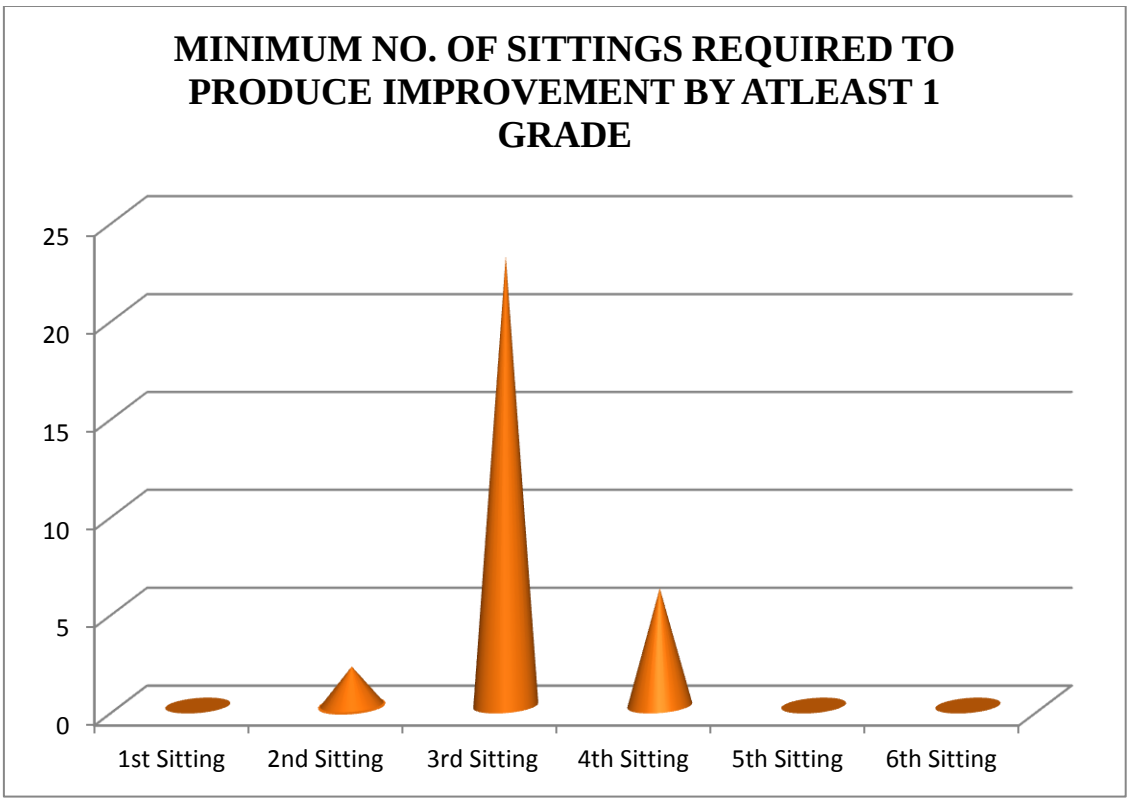
ASSESSMENT OF IMPROVEMENT AT THE END OF 4 WEEKS AFTER EACH SITTING

S. No.	NAME	AGE & SEX	INITIAL GRADE	GRADING AT THE END OF						Comment
				1ST Sitting	2ND Sitting	3RD Sitting	4TH Sitting	5TH Sitting	6TH Sitting	
1.	Arul	21/M	3	3	3	2	1			3 → 1
2.	David	28/M	4	4	4	3	3	2	2	4 → 2
3.	Shama	25/F	4	4	4	4	3	2	2	4 → 2
4.	Satya	28/M	3	3	3	2	2	2	2	3 → 2
5.	Anitha	29/F	3	3	3	2	2	2	2	3 → 2
6.	Shiva	24/M	2	2	2	2	2	2	2	No change in grade, but depth improved.
7.	Aiysha	26/F	2	2	2	2	1			2→1
8.	Priya	21/F	3	3	3	3	3	3	3	No improvement
9.	Akash	25/M	3	3	3	2	2	2	2	3 → 2
10.	Suresh	33/M	4	4	3	2	2	2	2	4 → 2
11.	Vinay	22/M	4	4	3	2	2	2	2	4 → 2
12.	Ramya	20/F	2	2	2	2	2	2	2	No change in grade, but depth improved
13.	Karthik	19/M	4	4	4	3	3	2	2	4 → 2
14.	Dinesh	27/M	4	4	4	4	3	2	2	4 → 2
15.	Praveen	27/M	3	3	3	2	2	1		3 → 1

S. No.	NAME	AGE & SEX	INITIAL GRADE	GRADING AT THE END OF						Comment
				1ST Sitting	2ND Sitting	3RD Sitting	4TH Sitting	5TH Sitting	6TH Sitting	
16.	Stephen	19/M	2	2	2	2	2	2	2	No change in grade, but depth improved.
17.	Swati	28/F	4	4	4	3	2	2	2	4 → 2
18.	Aasif	25/M	3	3	3	3	3	3	3	No improvement
19.	Karthikeyen	26/M	3	3	3	2	2	2	2	3 → 2
20.	Sarvanan	22/M	4	4	4	4	4	4	4	No improvement
21.	Sekar	21/M	3	3	3	2	2	2	2	3 → 2
22.	Yuvraj	28/M	3	3	3	2	2	2	2	3 → 2
23.	Kavitha	25/F	3	3	3	2	2	2	2	3 → 2
24.	Santosh	29/M	4	4	4	4	4	4	4	No change in grade, but depth improved
25.	Murugan	28/M	4	4	4	4	3	3	3	4 → 3
26.	Prasanth	26/M	3	3	3	2	1			3 → 1
27.	Govind	23/M	3	3	3	2	2	2	2	3 → 2
28.	Shwetha	25/F	3	3	3	2	2	2	2	3 → 2
29.	Senthil	27/M	4	4	4	3	3	2	2	4 → 2
30.	Kumar	21/M	3	3	3	3	2	2	2	3 → 2

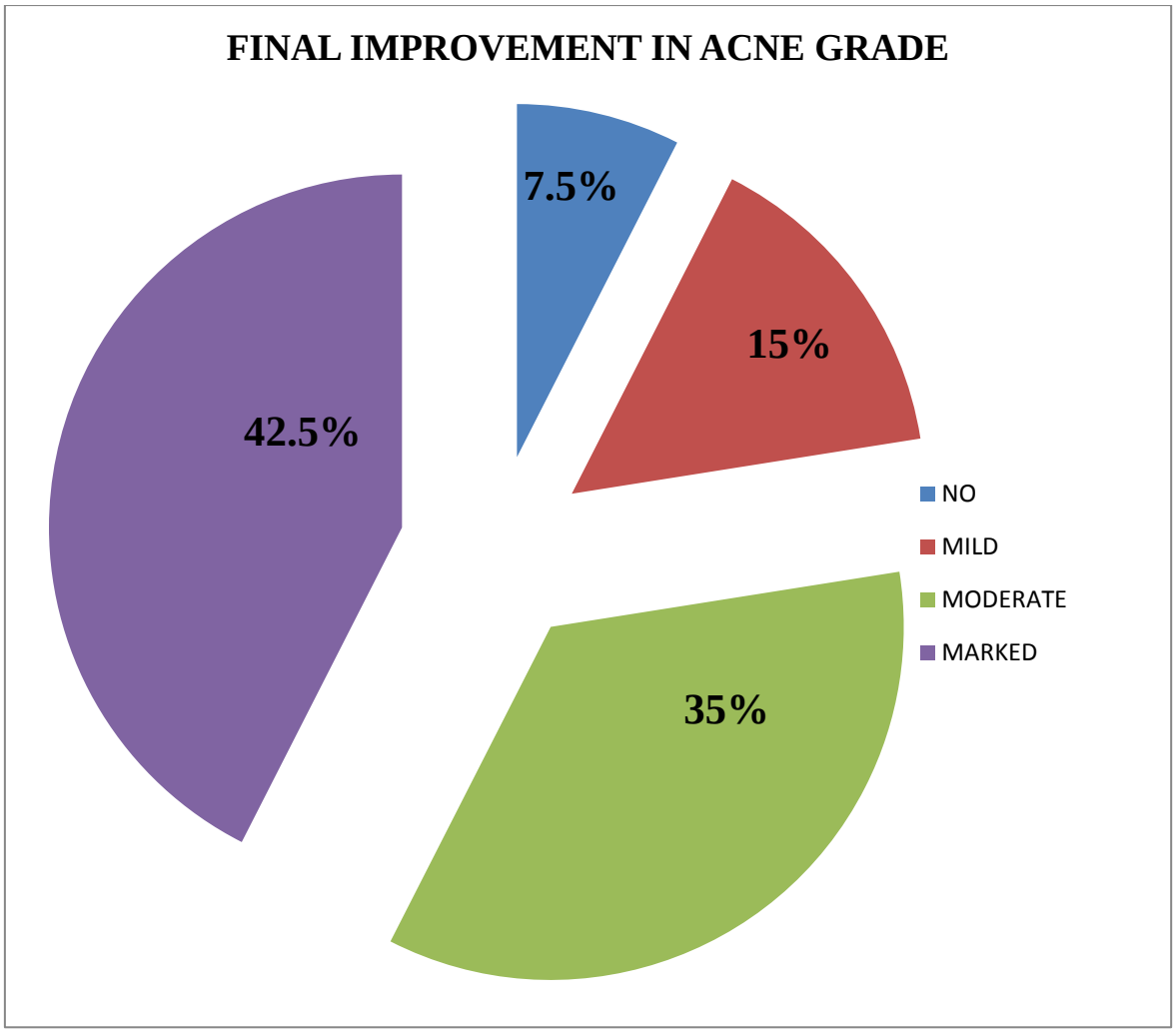
S. No.	NAME	AGE & SEX	INITIAL GRADE	GRADING AT THE END OF						Comment
				1ST Sitting	2ND Sitting	3RD Sitting	4TH Sitting	5TH Sitting	6TH Sitting	
31.	Vijay	21/M	2	2	2	2	2	2	2	No change in grade, but depth improved
32.	Rajsekar	23/M	3	3	3	2	2	1		3 → 1
33.	Selvam	26/M	4	4	4	4	4	4	4	No change in grade , but depth improved
34.	Arunraj	25/M	3	3	3	3	2	2	2	3 → 2
35.	Vinayak	29/M	4	4	4	3	3	2	2	4 → 2
36.	Bhaskar	24/M	3	3	3	2	2	2	2	3 → 2
37.	Keerthi	26/F	4	4	4	3	2	2	2	4 → 2
38.	Sohail	32/M	4	4	4	3	2	2	2	4 → 2
39.	Balaji	20/M	3	3	3	2	2	2	2	3 → 2
40.	Ilakiya	25/F	4	4	4	3	2	2	2	4 → 2

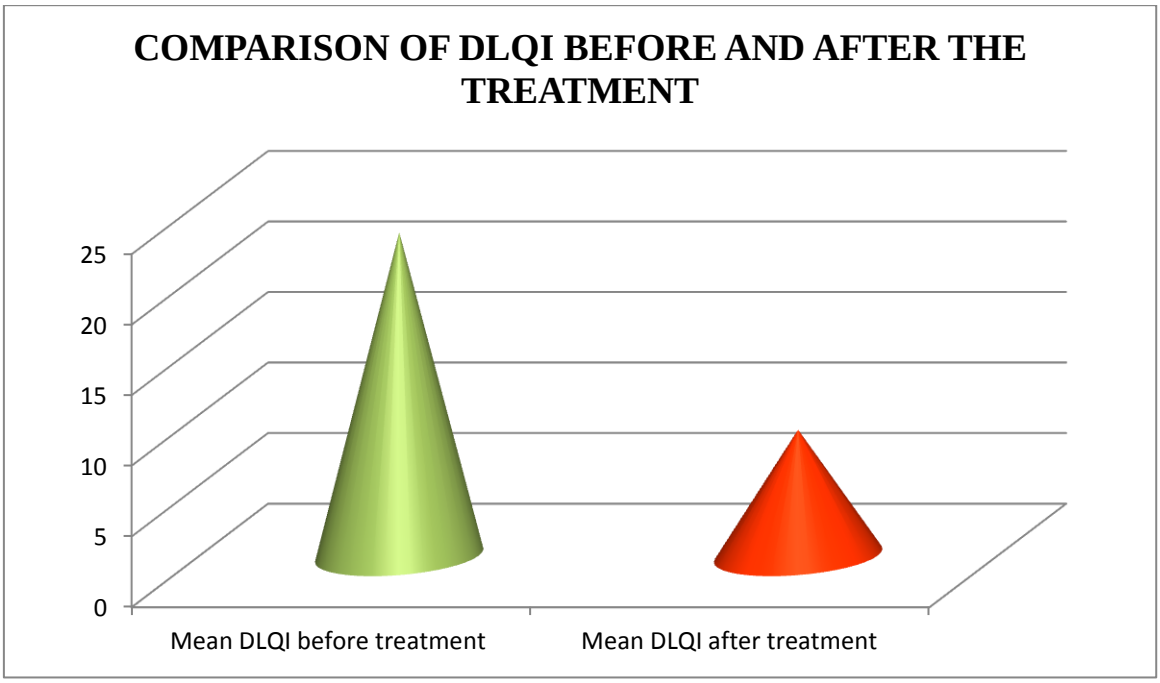
MINIMUM NO. OF SITTING REQUIRED TO PRODUCE IMPROVEMENT BY GRADE 1 OR MORE	NO. OF PATIENTS
1	0
2	2
3	23
4	6
5	0
6	0


MINIMUM NO. OF SITTINGS REQUIRED TO PRODUCE IMPROVEMENT BY ATLEAST 1 GRADE
25
20
15
10
5
0
1st Sitting
2nd Sitting
3rd Sitting
4th Sitting
5th Sitting
6th Sitting

Based on all the above observations, final improvement in patients was graded as following:

IMPROVEMENT IN GRADE	**NO. OF PATIENTS**
NO IMPROVEMENT	3
MILD(improvement was seen but difficult to say that grade changed)	6
MODERATE (those who decreased by 1 grade)	14
MARKED (those who attained grade1 or decreased by 2 grades)	17


FINAL IMPROVEMENT IN ACNE GRADE
7.5%
15%
42.5%
35%
NO
MILD
MODERATE
MARKED



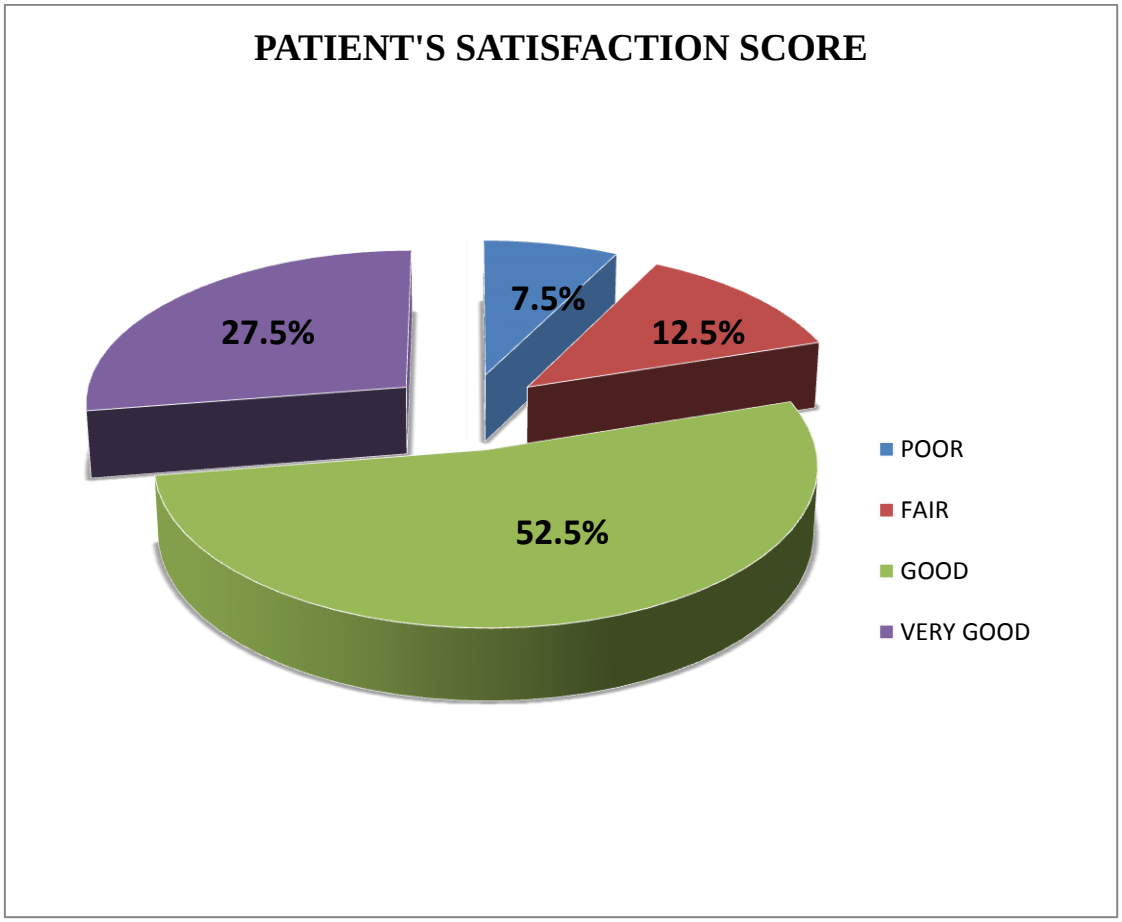
The mean DLQI improved by 61.13%.

At every visit patient was also asked about his satisfaction and whether he can appreciate any change. At the end of two months after 6 sittings of the procedure, final grading of acne scars done and the patient's satisfaction score was graded as below:

PATIENT'S SATISFACTIONSCORE	NO. OF PATIENTS
Poor- 0	**3**
Fair- 1	**5**
Good -2	**21**
Very good - 3	**11**
Excellent - 4	**0**

The patients were followed up monthly for a period of 6 months after the procedure to look for any complications and also to make sure that the results were not transient.

There were no drop outs in the study. All 40 patients continued with the procedure till the end.


PATIENT'S SATISFACTION SCORE
7.5%
12.5%
27.5%
52.5%
POOR
FAIR
GOOD
VERY GOOD

COMPLICATIONS:

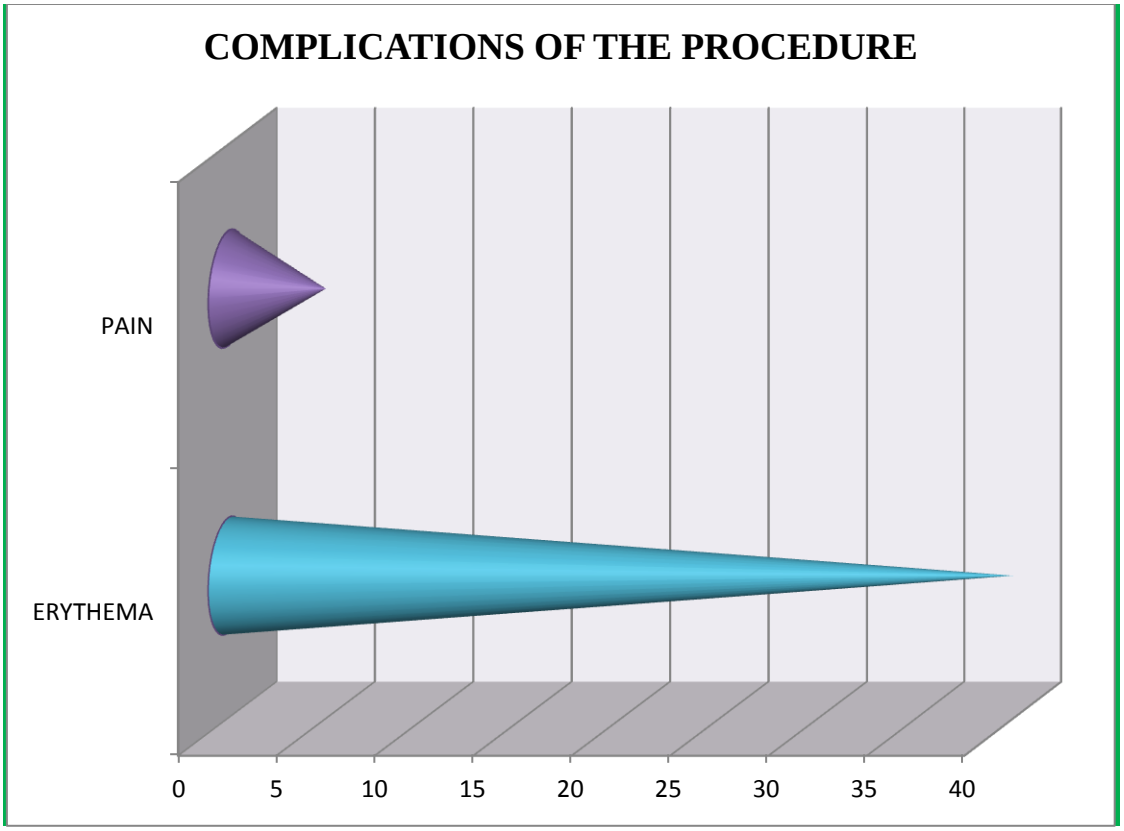
Practically the only complication seen was immediate post procedure erythema, which was seen in all the patients. The erythema however was transient and resolved in 6- 12 hours.

Even after proper application of topical numbing cream, around 5 patients complained of mild discomfort during the procedure.

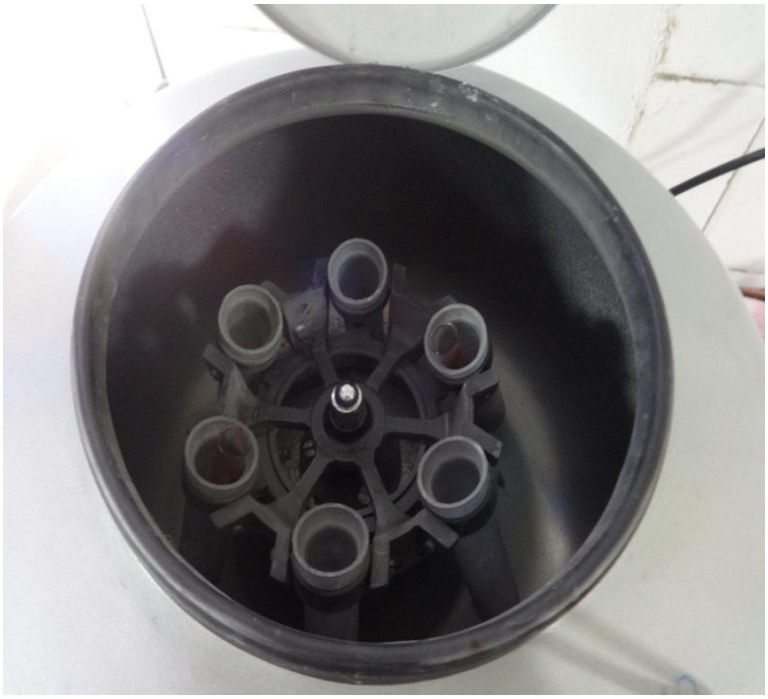
Apart from these, no other complication was noted.

TABLE 4: COMPLICATIONS

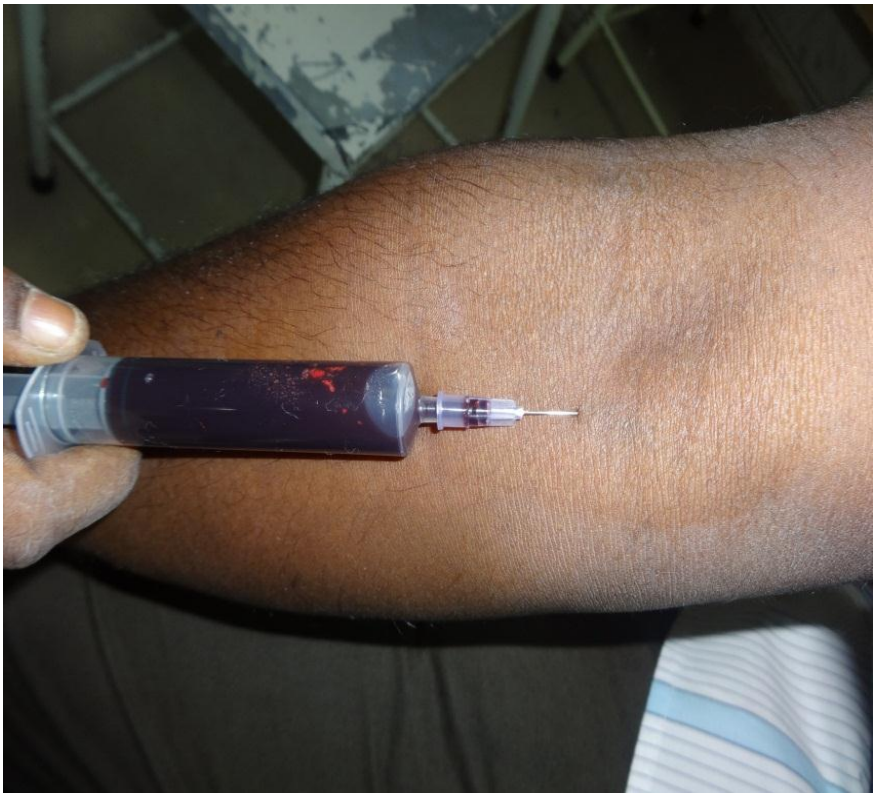
Complications	Number of patients
Post procedure erythema	40
Pain	5
Secondary infection	0

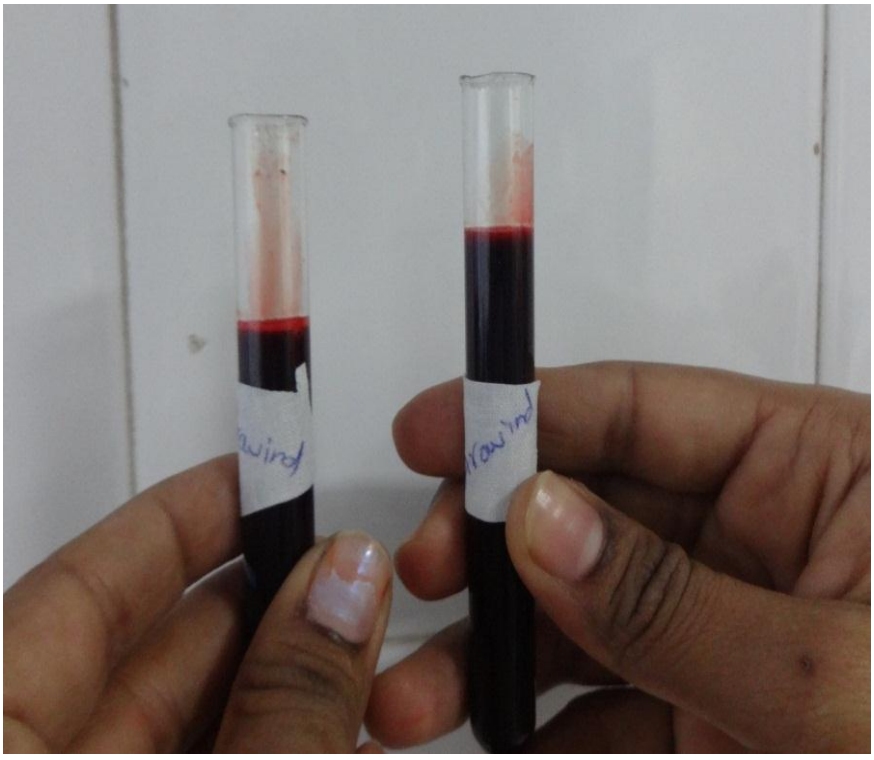

COMPLICATIONS OF THE PROCEDURE
PAIN
ERYTHEMA
0
5
10
15
20
25
30
35
40

CENTRIFUGE MACHINE

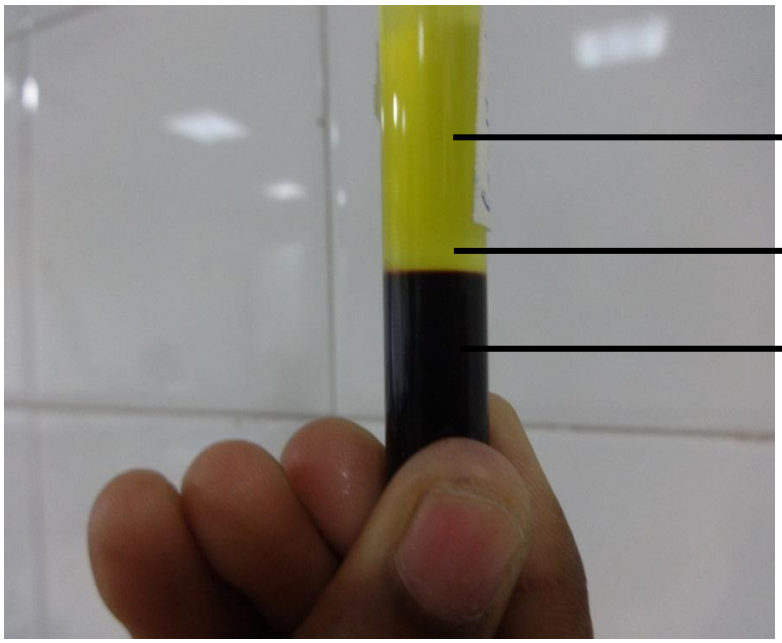


COLLECTION OF BLOOD FROM THE PATEINT

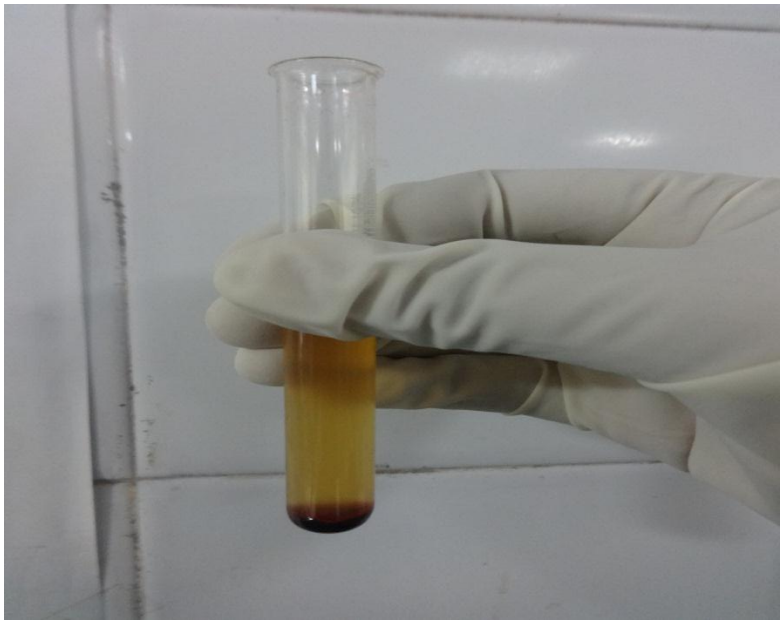




AFTER SOFT SPIN, SEPERATION OF PLASMA, BUFFY COAT AND RBCs



AFTER HARD SPIN PLATELETS SETTLE AT BOTTOM



PRP INJECTIONS INTO THE AREA TO BE TREATED

PRE- TREATMENT PHOTOGRAPH

AFTER 4 SITTINGS OF PRP MARKED IMPROVEMENT

PRE TREATMNENT PHTOGRAPH

AFTER 6 SITTINGS OF PRP MARKED IMPROVEMENT

SAME PATIENT 6 MONTHS POST TREATMENT,

EFFECT IS MAINTAINED

PRE TREATMENT PHOTOGRAPH

AFTER 6 SITTINGS OF PRP MARKED IMPROVEMENT

PRE TREATMENT PHOTOGRAPH

AFTER 6 SITTINGS OF PRP MARKED IMPROVEMENT

SAME PATIENT 6 MONTHS POST

TREATMENT, EFFECT IS MAINTAINED

PRE TREATMENT PHOTOGRAPH

AFTER 6 SITTINGS OF PRP MILD IMPROVEMENT

PRE TREATMENT PHOTOGRAPH

AFTER 6 SITTINGS OF PRP MODERATE IMPROVEMENT

DISCUSSION

PRP is a novel approach in the management of atrophic acne scars. The results are comparable with other approaches for acne scars if used singly. Out of 40 patients, 42.5 % patients(17) showed marked improvement in the grading of acne scars. It means they improved upto grade 1 OR there was an improvement by 2 grades. 35% patients (14) showed moderate improvement. In these patients grading of acne scar improved by 1. In 15% (6) patient although the grading did not change but there was visible improvement in appearance of the scars. In only 7.5% patients(3), no improvement was seen even after 6 sittings of PRP, who were definitely candidates for combination with other modalities.

Among the patients who showed improvement, 57.5% patients showed this improvement after 3rd sitting. In 15%, first improvement was seen at 4th sitting. In a small group of patients (5%), the effect could be appreciated at the end of 2nd sitting itself.

Around 52.5% patients put their satisfaction score as ‘good’at the end of procedure, while 27.5 % patients scored it as‘very good’. 12.5% patients gave a score of ‘fair’. Only 7.5% gave a ‘poor’ score.

The mean DLQI of the patients changed from 22.9 before treatment to 8.9 after treatment (61.13% improvement) .

Complications seen were only in form of transient erythema and pain. A follow up period upto 6 months showed that the results were permanent and there were no complications.

Most of the studies available have combined platelet rich plasma with conventional treatment for acne scars. However the individual effect of PRP has not been studied extensively.

The purpose of this study was to see the individual role of platelet rich plasma in the treatment of acne scars.

In a study done by Jiang Ting Zhu et al[69] ,combining Erbium Fractional LASER with PRP, 90.9% of the patients showed an improvement of >50%, and 91% of the patients were satisfied. However this study could not precisely tell about the role of PRP alone in remodelling of tissues.

Lee et al conducted a split-face trial that treated acne scars with PRP following ablative CO2 fractional resurfacing[60]. Fourteen Korean participants with acne scars were included in this study. They received one session of ablative CO2 fractional resurfacing, and then facial halves

were randomly assigned to receive treatment with autologous PRP injections on one side (experimental side) and normal saline injections on the other side (control side). Erythema edema on the experimental side improved faster than on the control side, and overall degree of clinical improvement was significantly better on the experimental side than on the control side.

Another study was done by Alessio Redaelli et al on Face & Neck revitalization using PRP alone[53], showed that PRP is a easy to perform & promising technique in face & neck revitalization & scar attenuation. Patients were treated with 3 sessions of PRP injections alone at interval of 4 weeks. A photograph score, patient's satisfaction score and doctor's satisfaction score all together showed an overall satisfactory result.

In a study Combining Use of Skin Needling and Platelet-Rich Plasma in Acne Scarring Treatment by Gabriella Fabbrocini et al[70], it was shown that the combined use of skin needling and PRP is more effective in improving acne scars than skin needling alone. The study showed that the microneedling apart from inducing new collagen synthesis made the PRP penetration easier, which helped in the action of the growth factors present in the PRP.

In our study, instead of using microneedling technique, PRP was directly injected into acne scars.

Bouwer et al also studied the effects of PRP mesotherapy in skin rejuvenation and scar attenuation.[71] They reported a very high 60% improvement in post acne scar with two sitting of PRP alone, results being visible at around 6 weeks after the procedure.

Procedures like dermabrasion[72] and ablative lasers have produced similar results.

However they always carry risk of pigmentation and scarring.

Prevention is always better than cure. So treatment of acne should be begun as early as possible to prevent formation of acne scars in first place.

Platelet rich plasma is a new generation approach to treatment of acne scars which utilises body's own platelets to heal the scars. It causes regeneration, rejuvenation and stimulates wound healing.PRP has been used in other medical fields for long, but relatively new in field of dermatology. It utilises body's own ability to heal itself. PRP is superior to other methods for acne treatment as it is safer, no chances of further scarring or damage and comparatively cost effective. It is relatively

painless when procedure is done after applying a numbing cream. Studies have shown the effectiveness of PRP when used in conjunction with other modalities. But there is scarcity of studies showing sole role of platelet rich plasma in acne scars.

CONCLUSION

In our study, male patients outnumbered the female patients attending the out patient department for the acne scars. This is in contrast to belief that females are more concerned about their physical appearance. The ratio for male : female was 3: 1.

The age group most commonly observed was 20-30 years. This is the time when the patient although gets rid of the acne lesions, but becomes distressed by its sequelae i.e. scars. Most of the patient's were students or working in sales and marketing fields.

Among the types of scars, it was rolling type of scars (45%) that out numbered others followed by combination of both rolling and boxcar scars.PRP holds good promise for the management of acne scars. Marked to Moderate improvement was seen in 77.5% cases, which is comparable with other modalities used for management of acne scars. In most cases the improvement became visible at the end of 3rd sitting.

Improvement in DLQI was also impressive with increase in mean DLQI from 22.9 to 8.9 and the patient's satisfaction ranged from 'very good to good' in around 80% cases.

It does not hamper daily activity of the patient as it is performed as out patient procedure. Entire procedure takes around 40-45 minutes. Minimal side effects like erythema and edema which subsides in 2-6 hours.

The procedure can be combined with other methods to get near total improvement in acne scars. Also the procedure is cost effective and doesn't require any surgical expertise. To conclude platelet rich plasma therapy is easy to perform and provides satisfactory results and that too with minimum side effects.

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ANNEXURE-1

GOVERNMENT STANLEY MEDICAL COLLEGE HOSPITAL
DEPARTMENT OF DERMATOLOGY

PROFORMA

NAME AGE SEX

OCCUPATION

ADDRESS

INCOME

CHIEF COMPLAIN

H/O PRESENT ILLNESS:

ONSET

DURATION

H/O AGGRAVATING FACTORS

H/O ANY TREATMENT TAKEN , ANY MEDICATION.

H/O ANY OTHER SYSTEMIC COMPLAIN.

PAST HISTORY:

ANY MEDICAL OR SURGICAL ILLNESS

FAMILY HISTORY:

PERSONAL HISTORY:

Smoking

Diet

Menstrual history

General physical examination

Systemic examination

Local examination :

Depth of scars

Type of acne scars

Grade of acne (Goodman and Baron Classification of acne scars)

Active acne present

DIAGNOSIS

INVESTIGATIONS:

CBC: HB:

TC:

DC:

ESR:

PLATELET:

LFT: S. BIL:

SGOT:

SGPT:

ALP:

STP:

S. ALB:

RFT: S. UREA:

S. CREATININE:

SCREENING for HIV and syphilis

CONSENT FORM

Mr/Miss/Mrs:
Age/Sex:
Address:

Phone:

I undersigned Mr/Miss/Mrs._____ have been explained regarding above said procedure in my regional language. I am fully aware of the possible side effects and risk involved in this procedure. I am also aware that this procedure may not always be successful and no guarantee can be made for successful outcome of the procedure.

I have been informed that this study will be done by Dr. Shubhra Shukla.

I have also been explained that during this procedure if any complication arises, it may be given any emergency treatment best suitable without asking my prior permission.

I further state that I have carefully read and understood all the information provided in this form and with full conscious mind, I hereby give my consent to be involved in this study.

I also give consent to take my clinical photograph required for the study purpose.

Signature/Right Thumb Impression of patient:

Signature/Thumb impression of the parent/guardian (In minors):

Witness:

Name: Signature:

Date:

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Assessment of efficacy and safety of platelet Rich Plasma (CRP) for treatment of acne scars

Principal Investigator : Dr.Shubhra Shukla

Designation : PG in MD(Derm)

Department : Department of Dermatology
Government Stanley Medical College,
Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 08.07.2013 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

22/8/13

MEMBER SECRETARY,
IEC, SMC, CHENNAI

MASTER CHART

S. NO	NAME	AGE	SEX	OCCUPATION	TYPE OF SCAR	DLQI		RESPONSE TO TREATMENT	SATISFACTION SCORE OF PATIENT	COMPLICATIONS		
						Before	After			TRANSIENT ERYTHEMA	PAIN	SEC. INFEC-TION
1.	Arul	21	M	Student	Rolling	23	7	MARKED	Very good	+	-	-
2.	David	28	M	Sales job	Rolling	21	10	MARKED	Good	+	-	-
3.	Shama	25	F	Student	Rolling	22	9	MARKED	Very Good	+	-	-
4.	Satya	28	M	Marketing	Boxcar	25	9	MODERATE	Good	+	-	-
5.	Anitha	29	F	Housewife	R + B	22	9	MODERATE	Good	+	-	-
6.	Shiva	24	M	Student	Rolling	21	10	MILD	Fair	+	+	-
7.	Aiysha	26	F	Marketing	R + B	21	8	MARKED	Very good	+	-	-
8.	Priya	21	F	Student	Boxcar	24	7	NONE	Poor	+	-	-
9.	Akash	25	M	Student	Rolling	25	10	MODERATE	Good	+	-	-
10.	Suresh	33	M	Business	R + B	23	9	MARKED	Good	+	-	-
11.	Vinay	22	M	Student	R + B	23	9	MARKED	Very Good	+	-	-
12.	Ramya	20	F	Student	Boxcar	25	8	MILD	Fair	+	-	-
13.	Karthik	19	M	Student	R + B	23	10	MARKED	Good	+	-	-
14.	Dinesh	27	M	Sales job	Rolling	24	10	MARKED	Good	+	+	-
15.	Praveen	27	M	Marketing	R + B	24	10	MARKED	Very Good	+	-	-
16.	Stephen	19	M	Student	R + B	25	9	MILD	Fair	+	-	-
17.	Swati	28	F	Housewife	R +B	21	8	MARKED	Good	+	-	-
18.	Aasif	25	M	Marketing	Rolling	22	8	NONE	Poor	+	-	-
19.	Kartikeyen	26	M	Engineer	Boxcar	24	10	MODERATE	Good	+	-	-
20.	Sarvanan	22	M	Student	Rolling	22	9	NONE	Poor	+	-	-

MASTER CHART

S. NO	NAME	AGE	SEX	OCCUPATION	TYPE OF SCAR	DLQI		RESPONSE TO TREATMENT	SATISFACTION SCORE OF PATIENT	COMPLICATIONS		
						Before	After			TRANSIENT ERYTHEMA	PAIN	SEC. INFEC-TION
21.	Sekar	21	M	Student	Rolling	21	10	MODERATE	Very good	+	-	-
22.	Yuvraj	28	M	Sales job	Rolling	22	9	MODERATE	Good	+	-	-
23.	Kavitha	25	F	Sales job	R + B	25	9	MODERATE	Very good	+	+	-
24.	Santosh	29	M	Business	Rolling	22	10	MILD	Fair	+	-	-
25.	Murugan	28	M	Marketing	Boxcar	23	8	MODERATE	Good	+	-	-
26.	Prasanth	26	M	Engineer	R + B	21	6	MARKED	Very Good	+	-	-
27.	Govind	23	M	Student	Rolling	22	10	MODERATE	Good	+	-	-
28.	Shwetha	25	F	Student	R + B	25	9	MODERATE	Very good	+	-	-
29.	Senthil	27	M	Sales job	R + B	23	9	MARKED	Good	+	+	-
30.	Kumar	21	M	Student	Rolling	24	8	MODERATE	Very good	+	-	-
31.	Vijay	21	M	Student	Rolling	22	10	MILD	Good	+	-	-
32.	Rajsekar	23	M	Sales job	Rolling	21	10	MARKED	Very good	+	-	-
33.	Selvam	26	M	Marketing	Boxcar	24	8	MILD	Fair	+	-	-
34.	Arunraj	25	M	Student	R + B	21	8	MODERATE	Good	+	-	-
35.	Vinayak	29	M	Business	Boxcar	23	9	MARKED	Good	+	-	-
36.	Bhaskar	24	M	Sales	Boxcar	25	10	MODERATE	Good	+	+	-
37.	Keerthi	26	F	Engineer	Rolling	22	7	MARKED	Good	+	-	-
38.	Sohail	32	M	Sales	Rolling	21	8	MARKED	Good	+	-	-
39.	Balaji	20	M	Student	R + B	21	10	MODERATE	Good	+	-	-
40.	Ilakiya	25	F	Student	Rolling	23	10	MARKED	Good	+	-	-