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Research Article

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The Effectivity of 15% TCA Superficial Chemical Peeling to Treat Comedos and Papulo-Pustules Acne Vulgaris

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ABSTRACT

Background: Acne vulgaris was very common self limitting disease, affected approximately 85% of adolesence, that was defined as a chronic inflammation of pilosebaceous units. It was characterized by the formation of comedones (as primarily acne lession), erythemathous papules and pustules, less frequently nodules and pseudocyst, and was accompanied by scarring in some cases that caused psychosocial problems.

TCA 15% was superficial chemical peeling, involved an application of exfoliating agents to the skin, resulting in controlling wound and destructing the portion of the epidermis with subsequent regeneration and reepithelialization within 3-5 days.TCA was the first line therapy for acne scar and skin rejuvenation.

Objective/Aim Study: To know the effectivity of 15% TCA superficial chemical peeling to treat comedos and papulepustules in acne vulgaris.

Research Design & Statistical Analysis: Cohort experimental Study - Wilcoxon Sign Rank Sum Test statistical analysis methods.

Material & Methods: One layer of 15% TCA superficial chemical peelings was applied. Clinical improvements were judged by counting acne lessions and classified the acne severity according to Global Acne grading System before and after treatment.

Result: There was statistically significant difference in clinical improvement of all type acne lessions before after therapy with 15% of TCA chemical peeling. The mean of difference of papulepustules before-after peelings was 5,14 (81,66%), comedos was 83,92 (85,23%) and the total acne lessions was 77,07 (86,79%). The mean of difference of GAGS acne score before-after peeling was 13,07 (74,75%).

Discussion: This research proved that one layer of 15% TCA superficial chemical peeling was statistically and clinically effective and good to treat all type of acne vulgaris. It was the best comedolytic activity and good to treat inflammatory/papulepustules acne lession. The goal therapy of acne vulgaris: removed plugging of the pilar drainage, reduced sebum production, treated bacterial and fungal colonization, and prevented from scarring could be solved by 15% TCA superficial chemical peeling.

It improved the depth contour and caused softening associated scars by their action on collagen remodelling and stimulation of new collagen activity, reepithelialization, regenerated compact epidermis that improved light reflection, eliminated dermal melanin and prevented transfer melanin to keratinocytes that improved skin textural and fine line, glowed, rejuvenated, lightened and minimized PIH. It decreased skin pH and TEWL and improved skin barier permeability.

15% TCA superficial chemical peeling was good and well tolerated methods for acne therapy, now considered as the single main acne therapy or could be combined with other therapy to treat acne chronicity and solved resistance problems to antibiotics and antifungi.

Keywords: Acne vulgaris, 15% of TCA superficial chemical peeling effectivity

Introduction

Acne vulgaris was very common self limitting disease, affected approximately 85% of adolesence, that was defined as a chronic inflammation of pilosebaceous units. It was characterized by the formation of comedones (as primarily acne lession), erythemathous papules and pustules, less frequently nodules and pseudocyst, and was accompanied by scarring in some cases that caused psychosocial problems. Global Acne Grading System classified the severity of acne vulgaris into 4 types:

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mild (Score 1-19), moderate (Score 20-29), severe (Score 30-39), very severe (Score>39), based on the kind of acne lession 0=nolession, 1=comedo,2=papule,3=pustule,4=nodulocystic) X Factor (location of acne lession Forehead=2,Nose=1, Chin=1, Left cheeck=2, Right Cheek=2, Chest & upper back=3).

Four major factors were involved in the etiopathogenesis follicular hyperkeratinization, increased sebum production, abnormality of microbial flora and inflammation process. The goal of therapy was removed plugging of the pilar drainage, reduced sebum production, treated bacterial colonization, prevented from scaring. The complications were acne scar, persistent hyperpigmentation, pyogenic granuloma formation, persistent swelling, gram negative bacteria folliculitis, bacterial and fungal folliculitis as secondary infection, resistances to antibiotics.

Superficial chemical peeling/chemical resurfacing/chemoexfoliation/chemosurgery involved an application of one or more exfoliating agents to the skin, resulting in the destruction of portion of the epidermis and might reach the papillary dermis (dermal epidermal interface) with subsequent re-epithelialization and regeneration within 3-5 days. This produced controling wound.

The goal therapy of acne vulgaris removed plugging of the pilar drainage, reduced sebum production, treated bacterial and fungal colonization, and prevented from scaring could be solved by 15% TCA superficial chemical peeling as one of acne vulgaris treatment choices. It had keratolityc effect by dissolved intercellular cement and reduced corneocyte adhesion. It acted as comedolityc agent, so decreased sebum production and free fatty acid that flourished bacterial and fungal colonization and reduced inflammation, so it acted as anti-inflammation. It improved the depth contour and caused softening associated scars by their action on collagen remodelling and stimulation of new collagen activity. It induced re-epithelialization, thinning and regenerated compact epidermis which improved light reflection, eliminated dermal melanin and prevented transfer melanin to keratinocytes, resulted in skin textural and fine line improvement, glowing, rejuvenating, lightening and minimizing PIH.

TCA 15% was superficial chemical peeling, considered as single main acne therapy or adjunctive therapy in acne, frequently added to other acne therapy, and as first line therapy for acne scar and skin rejuvenation. In high concentration was good for treating acne scar (CROSS/ Chemical reconstruction of Skin Scars technique).

The purpose of this research was for sharing experience in treating acne vulgaris, the chronic pilosebaseus infection that difficult to be eradicated because of the disease chronicities that caused many resistance problems to antibiotics. The 15% of TCA Superficial Chemical Peeling was one of the main acne treatment choices that solved antibiotic resistance problems.

Acne Vulgaris

Definition

Acne vulgaris was a very common self limitting disease, that was seen primarily in adolescent. It was defined as a chronic inflammation of the pilosebaceous units [1-4]. Acne was not infectious [3].

Incidence

Acne vulgaris affected approximately 85% of young people [1,3,4]. The age of onset was at puberty, typically 12-15 years, but could firstly appeared at 25 years old [1,4]. Ihe peak insidence of acne vulgaris was in 17-21 years (17-18 years in female and 19-21 years in males) [4]. Acne vulgaris was more severe in males than females [1]. The lower incidence of acne vulgaris was in Asians and Africans [1]. Acne in Black Americans were less evident than white Americans [3].

Diagnosis & Clinical Manifestation

Acne vulgaris was characterized (diagnosed) by the formation of comedones (open/black head and closed/white head), erythemathous papules and pustules, less frequently nodules and pseudocysts (could been ruptured, reencapsulated, inflammed and formed abscesses), draining sinus tracts (round isolated single nodules and cysts coalesce to linear mounds), that was accompanied by scarring in some cases [3]. Acne vulgaris lessions were polymorphic due to inflammation process of acne lessions [4]. Comedones were the primarily lessions of acne, but they were not unique and could been found in other skin disease like senilis comedo [1]. The predilection of acne vulgaris were on the face, trunk, upper arms and buttock.1 Seborrhea of the face and scalp frequently presented and could been severe [1].

Duration of lesion: The duration of lession was weeks to months [1].

Season: Acne vulgaris was worsen at winter and fall [1].

Symptom: It was Itchy and pain especially in nodulocystic type [1]. Itchy was rare. It could be found in early phase of acne or in succesfully treatment cases. Itchy was caused by releasing histamine like substances that were produced by P acnes that were killed by treatment [4]. Pain was also rare, could been found in patients with nodule and sinus espescially on the trunk [4].

Classification

Fitzpatrick classified acne vulgaris as non-inflammatory lessions (white head and black head comedos) and inflammatory lession (papules, pustules, nodules, cysts) [1]. Plewig and Kligman in 1975 classified acne vulgaris in 3 types: comedonal, papulopustular and conglobate [5]. Cunliffe classified the severity of acne vulgaris according to the number and types/ kinds of the lession into 4 types of acne vulgaris mild, moderate, severe and very severe acne vulgaris [4]. The types of lession were comedones, papules/pustules, nodules/cysts/sinus tracts, inflammation and scarring [4]. This case report classified and judged the severity and after treatment clinical improvement of acne vulgaris based on Cunliffe classification criteria.

Laboratory Examination

No laboratory examination was required [1]. In the majority of acne patients had normal hormonal levels [1]. If endocrine disorders were suspected (especially in patients who had clinical manifestation of hyperandrogenism like irregular menses, hirsutism, hoarse voice, alopecia androgenism), determined free testosterone, follicle stimulating hormone, luteinizing hormone and DHEAS to exclude hyperandrogenism and polycystic ovary syndrome [1,3,4]. Recalcitrant acne could also be related to congenital adrenal hyperplasia (11β atau 21β hydroxylase deficiency) [1].

Etiopatogenesis

Acne vulgaris was multifactorial disease of pilosebaceous follicles. The important patophysiology of acne vulgaris were follicular hyperkeratinization, increased sebum production, P acne colonization, Inflammation [1].

Four major factors were involved in the etiopathogenesis [1-4].

Follicular hyperkeratinization and cornification of the pilosebaceous duct

It was not been known whether the initial trigger for acne was seborrhoea or ductal hyperkertanization or both [4].

Several factors that might been important as ductal hypercornification/follicular hyperkeratinization mechanism were [1-4].

a. Abnormal response to androgen
b. Abnormal lipid composition of the ductal corneocytes (local deficiency of linoleic acid)
c. Local cytokine activity (IL1α)

Microbial factors

Androgen that quantitatively and qualitatively normal in serum stimulated sebaceous glands to produce more sebum, there was high sebum secretion rate [1]. Essential fatty acid linoleic deficiency was characterized by inducing follicular hyperkeratosis, impacting of corneocyte and decreasing epithelial barrier function, low level linoleic acid led comedogenesis [1,3,4]. The changing in sebum secretion or composition (could flourished microorganism growth that activated immune system) could led to release of IL 1α by follicular keratinocytes, which in turn could stimulated comedogenesis.1 Pro inflamatory cytokine stimulated abnormal keratinocyte proliferation and differentiation revealed obstruction [1,2]. Follicular plugging was formed and would prevent the drainage of sebum and androgens [2]. There was follicle impaction and distention, formed comedos that were disrupted and ruptured, there was leakaged of follicular materials that induced inflammed lessions [2,4].

The early hypercornification of acne was not been initiated by bacteria, but later there were microbacterials grew and bacterial lipases converted triglycerides to free fatty acids, there was changed of sebum composition and diluted linoleic acid concentration that led hypercornification (follicular hyperkeratosis1) and comedogenesis [4].

Comedones represented as the retention and hyperproliferation of ductal corneocytes in the duct [3,4]. There was accumulation of multiple corneocytes in the duct could been caused by either an increased in production of basal keratinocytes or failured of the keratinocytes to be expelled from the duct [4].

Ductal hypercornification hystopathologically was presented as microcomedones and clinically as blackheads and whiteheads [3]. There was a signifficant correlation between the severity of acne and the number and size of follicular casts in comedogenesis [3]. There was an increasing in proliferation of ductal keratinocytes of non-affected and affected follicles. Hystologically microcomedos were found in normal nearby sites of acne and area that was affected with acne [3]. The primary abnormality that led to hypercornification was not been related to change in keratin expression, hypercornification and comedogenesis might been related to failure the ductal corneocytes to separate [3].

The primary changed in the sebaceous follicle in acne was an alteration in the pattern of keratinization within the follicle [1]. Normally keratinous material in the follicle was loosely organized. In ultrastructural level, there were many lamellar granules and relatively few keratohyaline granules. Comedo formation was firstly formed in the lower portion of follicular infundibulum (infrainfundibulum) [1]. The keratinous materials were denser, the lamellar granules were less numerous, keratohyalin granules were increasing and some of cells were containing amorphous materials (which were probably lipid). were generated during the process of keratinization [1]. Kinetic studies demonstrated that there was an increasing in cellular turn over in comedones [1].

Corneocytes frequently contained about 20 % water but they were varying markedly with age [4]. The swelling of the epidermis was caused by hydration, that followed prolong soaking of the skin, particularly in warm water, was familiar in most people. Corniffied epithelium of the sebaceous follicle became hydrated, that might increase sebum outflow resistance by reducing the size of the pilosebaceous ostium [4]. This obstruction was associated with a decreased in outflow of sebum [3]. Acute obstruction of a particular pilosebaceous duct might then occured and thus precipitated acne [4]. It explained tropical acne and premenstrual acne flared [3].

Comedogenesis was also related to the potential importance of what was called the sebolemmal sheath [3]. It had been suggested that the excretion of products from the sebaceous gland was occured through an organized acellular tubular conduit-the sebolemmal sheath was produced by sebaceous duct cells. The rupture of this sheath might contribute to comedogenesis [3].

Abnormal response to androgen influenced hypercornification

The evidence was accumulating to propose that androgens (a male steroid hormone such as testosterone) might play an important role in comedogenesis [3]. The cells of pilosebaceous duct had androgen receptors and 5α reductase type I (enzym that converted testosterone to DHT) was also present in this cell [3].

Androgen were known to regulate the development of sebaceous gland and sebum production

Androgen might play indirect at the follicular hyperkeratinization was supported by some.

Obsevations

1. Androgen receptors had been localized to the outer root sheath of the infrainfundibular region in the follicles.
2. The formation of follicular cast reduced in patients that was treated with anti-androgen.
3. Each of the key enzyme involved in androgen metabolism had been identified in the follicles.

Abnormal lipid composition in keratinocyter duct influenced hypercornification

Follicular hyperkeratinization might related to a local deficiency of linoleic acid, production of IL 1α within the follicle or

possibilly the effect of androgens (high sebum secretion rate) [1]. Low essential fatty acid linoleic caused:

- Inducing follicular hyperkeratosis/hypercornification (which might parallel with the increased scale that was found in comedo) [1,3].
- Impacting of corneocytes that formed comedones [4].
- Decreasing epithelial barier function (which might make the comedonal wall more permeable to inflammatory substances) [1,3,4].

Membrane coated granules were probably more related to barrier permeability than cell separation and that were decreased in commedones [3].

In examination of polar lipids recovered from comedone showed that the acyl ceramides were contain only 6% linoleic acid among esterified fatty acids, compared with 45% in normal human epidermis [3].

Linoleic acid concentration was decreased in acne patients' sebum [3].

Other lipids had been incriminated, there were free fatty acids, squalene, squalene peroxides, oleic acid, isopropyl niristate, liquid parafin, wax ester, ceramid, linoleic acid. Low ceramides and low-level linoleic acid essential fatty acid in ceramide had been blamed for inducing comedones [3,4]. There was correlation between lipid peroxidase levels (an oxidative degradation of lipids resulting in cell damage) and the size of comedos. There were low level of linoleic acid and high sebum level in acne patients [4].

UVA radiation in lipid substance composition (squalene, oleic acid, isopropyl nyristate, liquid paraffin) induced comedogenesis [4]. There was high sebum flowed that produced a local deficiency of vitamin A in the duct that induced ductal cornification [4]. Then the changing in sebum secretion or composition could led to release of IL 1α by follicular keratinocytes, which in turn could stimulated comedogenesis [1].

The primary site of the developing comedone in the sebaceous follicle in acne vulgaris was at the level of the infrainfundibulum [4]. It was proposed that at the time of cell division, when the sebaceous cells still had a contact with the basement membrane, they still had and access to circulating lipid, including linoleate [4]. Once sebum synthesis began, no further lipids were accepted from circulation, so that more sebum was synthezised per cell, and linoleate content would been diluted [4]. This linoleate content would been released at the time of final cell ruptured and incorporated into various lipids in proportion to be relative rates (linoleic acid was diluted by sebum and the concentration would been low), at which these lipids were being synthesized at the time of cell ruptured [4]. Linoleic acid was essential fatty acid that could not been synthesized by human cell tissue [3,4].

The pilosebaceous unit comprised a matured epiuthelium and developed sebocytes through which the hair and sebum passed. Anatomically the pilosebaceous unit was divided into smaller unit's infundibulum (acroinfundibulum and infrainfundibulum) and sebaceous duct [4]. The sebocytes rest on the basement membrane that were contiguous with the dermis and extending from this basal layer into the central part of the gland. The sebaceous gland was a holocrine gland, the secretion was the result of self-destruction of the sebocytes. The nucleus was moved to the periphery of the cell. The cell then entered the pilosebaceous duct. The sebum was secreted, then it was moved up with desquamated corneocytes and presented microbes to the surface [4].

Local cytokine influenced comedo formation

Inteleukine 1α was found in comedo, it was important in comedogenesis and it was produced by keratinocytes of the duct [3]. It was proved by in vitro study. This effect could be blocked by Interleukine 1 antagonists and the formation was totally disrupted by EGF (Epidermal Growth Factor) [3,4].

Microbial factors influenced duct hypercornification

Two studies had failed to incriminate bacteria in the initiation of comedones, and it was proved by the fact that there were no bacterias that had been shown in some early comedones. Ultrastructurally and cultures of some early non inflamed biopsy material that were taken from lessions were sterile [3,4].

P. acnes was not involved in the initiation of comedones but might been involved in the later stages of comedogenesis [3,4]. The early hypercornification of acne was not been initiated by bacteria, but later there were bacterias colonization that produced lipase that converted triglyserida to free fatty acid, and increasing sebaceous free fatty acids would been changed sebum composition and diluted linoleic acid concentration that led hypercornification (follicular hyperkeratosis), corneocytes impaction that formed comedo and decreasing epithelial barier function that increased permeability of comedonal wall [1-4].

Biopsy and culture of early non inflammed lessions had shown that 30% of these were without bacteria suggesting that ductal bacteria were not needed for initiation of cornification [3]. Electron microscopy of early non inflammed lessions that were taken from prepubertal and early pubertal individual had demonstrated few or no bacteria [3]. Quantification of bacteria from comedones suggested that follicular colonization might been unrelated to comedogenesis [3].

Increased sebum production

Normal or abnormal androgens stimulated sebaceous glands to produce more sebum or there was end organ androgen hypersensitivity response in normal hormonal level of acne vulgaris that made bacterial and fungal were flourished [1,3,4].

There was much debated concerning the prime trigger to acne, it was the increased of sebum production or formation of comedones or both abnormalities developed paralel in the same acne prone pilosebaceous follicle [4]. Lipid composition influenced comedones formation [4].

Sebum excretion increased in acne patient than normal people and the increasing of sebum exctretion was equally with acne severity [3].

Increased production of sebum in acne patients was explained as 4 possibilities [4].

1. An elevated level of circulating hormone that was caused by an abnormal pituitary drive

2. An abnormal increase in the production of androgen in the adrenal and gonad,
3. An end organ hyper response of the sebaceous glands to normal circulating level of hormone.
4. Combination

In most of acne patients had no hormonal misfit. Most patients in clinic did not require investigations of sex hormones simply because the patients seem otherwise normal, they responded well to an appropriate treatment reasonablly and thus did not need detailed endocrinological examination [4]. There were rare cases that acne female patients had clinical sign of abnormal hormonal level like excessively hairy, hoarse voice, irregular menses and they got on well with the men and could been pregnant. In this patient could been found an elevation levels of circulating androgens or an abnormal pituitary drive [4].

There was an end organ hyper response of the pilosebaceous unit to normal levels of circulating androgens. And it was supported by the finding that the sebaceous glands in acne prone areas function differently to those in non-prone areas, so acne could be found only on the trunk and none on the face, or acne just on the face and none on the back and chest [4].

A connection between acne and high rates of sebum secretion was supported by at least 3 types of evidence [1].

1. Children did not get acne during the age range from approximately 2-6 years, when sebum secretion was extremely low.
2. Average rates of sebum secretion were higher in individuals with acne than those without acne.
3. Treatment that reduced sebum secretion (such as estrogen, 13 cis retinoic acid) improved acne.

Increased sebum production was presented as patient`s seborrhoea (greasy skin) [3]. Active sebaceous glands were a prerequisite for the development of acne. Acne patient's male and female, excreted on average more sebum than normal subjects, and the level of sebum secretion correlated reasonably well with the severity of the acne [3]. Sebaceous activity was predominantly dependent on androgens sex hormones of gonadal or adrenal origin [3]. Abnormally high levels of sebum secretion could be thus resulted from high overall androgen production or increased availability of free androgen, because of a deficiency in sex hormone binding globulin (SHBG) [3]. Equally they could involve an amplified target response mediated either through 5α reductase of testosterone or an increased capacity of the intracelluler receptor to bind the hormone [3].

Lawrence et al found that only 41% of the acne patients had free testosterone level above normal. Lucky et al measured a number of androgens and their precursors as well as, and found that 52% of non-hirsute women with acne had at least one abnormal hormone level. Darley et al found high sebum testosterone in 26%, low SHBG in 45% and high prolactin in 45% of 38 woman with acne However 24% of the total had no hormonal abnormality [3]. Peripheral androgen metabolism might be important for example increased androsterone metabolism had also been reported in normo androgenic females [3].

In some published papers, it would seem that androgenic hormonal balance was disturbed in 50-75% of female acne patients [3]. However, this had not been established that it was the critical factor, and at least a quarter of all cases remain unexplained [3]. The development of acne was simply related to systemic hormone levels. But in general, acne patient had not frequently had endocrine misfit [3].

The acne did not occur simultaneously on all susceptible sites was consonant with the finding that sebum secretion was varies from follicle to follicle. In acne patients, there were marked heterogenicity in individual follicular sebum excretion [3]. This suggested that certain follicles might been proned to acne [3].

An enhanced peripheral response should be considered as a factor in many subjects [3]. The possible role of increased 5α reductase of testosterone to its more active metabolite was indicated, both by the deminstration that sebaceous glands in acne prone regions showed abnormallity high 5α reductase activity in vitro, and by the finding of abnormally high ammount of 5 alfa androstenediols in the urine of female acne patients [3]. There were 2 forms of 5α reductase, type I and type II, and the type I 5α reductase was more relevant. The activity of type I 5α reductase in isolated sebaceous glands also supported the end organ hyperresponsiveness theory for acne [3]. Androgen action on the sebaceous gland might been independent from serum hormone levels [3].

There was possibility that other hormones affected the sebaceous glands, either directly or by enhancing their response to androgens [3]. Low sebum excretion rate was low in individuals with isolated growth hormone deficiency, but this endocrinopathies was rare [3].

Sebum consisted of mixture of squalene, wax and sterol esters, cholesterol, polar lipid and triglyserides. As the sebum moved up the duct, bacteria especially P acnes hydrolized the triglycerides to free fatty acids, which eventually appeared at the skin surface. Free fatty acid fraction of the sebum was considered to be important in the causation of inflammation [1,3]. Triglycerides fraction in sebum was probably responsible for acne [1].

The role of individual lipid components in causing acne was uncertain. Lipid might be involved in ductal hypercornification or might been essential to the growth of bacteria [3]. Sampling of skin surface lipids had shown that patients with acne tended to have higher levels of squalene and wax esters, and lower levels of essential fatty acids linoleic acid, and a more frequent occurences of particular free fatty acids [3]. Linoleic acid was significantly reduced in ductal hypercornifications [3]. Linoleic acid levels were signifantly decreased in acne patients and there was inverse relationship between sebum secretion and linoleic acid esential fatty acid concentration of sebum [1]. Linoleic acid could not be synthesized in mammalian tissue and its concentration was diluted by subsequent endogenous lipid synthesis in sebaceous cell [1].

In was unclear, why elevated rates of sebum secretion led to acne. The triglyceride fraction of sebum, which was unique to humans, was probably responsible for acne. The bacterial population of the follicle hydrolized triglycerides to fatty acids, which eventually appeared on the skin surface. In the past, the free fatty acid fraction of sebum was considered to be important

in the causation of inflammation, but in recent years it had become evident that there were probably other more important causes of inflammation [1].

The sebaceous glands produced a considerable amount of sebum in the first 3 months of life, which then gradually reduced to zero at 6 months of age. This neonatal stimulus was likely to be an effect of the fetal and neonatal adrenal androgens. After 6 months of age the sebaceous gkands remained quiscent until early adrenarche. At adrenarche, around 7-8 years, there was an increased in adrenal androgens, in particular dehydroepiandrostenedione, with the resultant increased in sebum excretion. In the early pubertal years there was a further increased in adrenal androgens and gonadal androgen stimulus to the sebaceous gland. There was an obvious increased in greasiness of the skin (seborrhoea), even in subjects who did not have acne. The sebaceous gland was under endocrine control. The main stimulus to the sebaceous glands was androgens. The pituitary had an important role in controlling the androgen production via the adrenals and gonads. The adrenals in particular produced dihydroepiandrostenedione and the gonads in both sexes produced testosterone. The circulating androgens, in particular testosterone were bound to the sex hormone binding globulin and it was the 1-2% of free testosterone was dictated sebaceous gland activity [4].

In both sexes, independent of the presence or absence of acne, there was a gradual increased in sebum excretion from puberty and beyond reaching a peak at about the age of 16-20 years. Thereafter the level remained constant until there was a gradual decreased from about 40 years onwards in women and from about 50 years in males. In general, the sebum exretion rate (SER) in men was signifficantly higher than in women [4].

Patients with acne also had seborrhoea indeed many patients complained that as acne developed so there was an increased greasiness of the skin and on the scalp. There was a reasonable correlation between the amount of sebum production and the severity of acne. There was evidence that those subjects with seborrhoea and acne had a higher number of sebaceous lobules per gland. Indeed, one of the disappointing features of acne therapy with most therapies were the fact that despite an improvement in the acne the sebaceous was persisted. But in Dianette (cyproterone acetatate+ethinyl estradiols) and isotretinoin therapy, there was a significant reduction in sebum excretion and acne improvement [4].

Measurements of sebum excretion also showed that individuals with acne produced more sebum than individuals who had never had acne. There was a gradual decreased in sebum excretion beyond the age of about 40 years. Thus, reduction in sebum alone was not accounted for resolution of acne [4].

There were differences of the lipid composition between the skin surfaces and in the sebaceous glands. Skin surface lipid composition had less triglycerides and more free fatty acids levels, and equally same levels of wax esther, squalene, cholesterol esters and cholesterol. It was caused by lipolityc enzymes that were produced predominantly by U that hydrolized triglycerides into free fatty acids when the sebum was moved up from the pilosebaceous duct [4].

The abnormality of the microbial flora

Bacterial and Pityrosporum ovale `s lipase hydrolyzed triglycerides to free fatty acids that flourished bacterials and Pityrosporum ovales themselves [4]. There was lipid composition changing and free fatty acid would mark inflammation process [3,4]. Free fatty acid was comedogenic [4]. Bacterial and fungi were bound to the receptor of monocytes, keratinocytes, perifollicular and peribulbar macrophages, sebocytes, langerhans cells and other inflammatory cells (through TLR2 Receptor or others) and T lymphocytes (through CD4) than produced proinflammatory mediators (IL1α, TNFα, etc) that led to an inflammatory response [1-6]. P acnes induced TLR 2 Receptor expresion and play role in acne inflammation [6].

Adolescence and its attendance seborrhoea were associated with a significant increase in P acnes [3]. But there was a little or no relationship between the number of bacterias on the skin surface or in the duct with the severity of acne [3]. But in other books Cunliffe said that there was a correlation between the reduction in P acnes counts and the clinical manifestation of acne [4]. The development of resistance to P acnes might equated with clinical failure to treat the acne [4]. There was no P acnes colonization in non-acne vulgaris patients [3]. P acnes colonization was at anterior nares [4]. And P acnes were important in acne pathogenesis [1].

Sebum excretion rate and ductal cornification correlated well with clinical severity [3]. Acne was not infectious [3]. The three major organisms were isolated from the surface of the skin and the duct of patients with acne were Propinibacterium acnes, Staphylococcus epidermidis and Malassezia furfur/ Pityrosporum ovale [3]. There were three major subgroups of the Propionibacterium: P acnes, P granulosum and P avidum [3]. Almost certainly P acnes and to lesser extended P granulosum were the most important [3]. Nevertheless, as they lived in association with the Staphylococcus epidermidis and Malassezia furfur, three organisms had probably some control over the growth of P acnes [3]. And Staphylococci were the first organism that colonized the normal skin people [4].

Staphylococcus epidermidis were found as comensal (normal colony at nares, head and axilla) and patogen (as chronic nosocomial infection that infected through contaminated stuff in cardiac cathetherization or other procedures). It was difficult to be eradicated, it had high resistances, it was easy to be infected again after it was treated (by hands or contaminated stuff) and it was clinically found as chronic infection. But this colonization inhibited Staphylococcus aureus virulencies [7].

Pityrosporum ovale was lipophilic, saprophytic, budding, unipolar, dimorphic gram positive, double walled, oval to round yeast. They were normal part of the follicular skin flora, and alteration in flora caused uncontroled growth of yeasts and would been pathogenic [4]. They needed free fatty acid for survival (they had lipase that hydrolized triglyceride to free fatty acid). They were found in stratum corneum and in pilar follicles in areas with increasing sebaceous gland activity such as chest and back [8].

P acnes were gram positive, non-motile, rods that tended to be irregular when the first isolated - some were short branching

and required free fatty acid to colonize [3,4]. P acnes should be clumped, free fatty acid aided clumping, and so bacterial lipases might be necessary for clumping and for ductal colonization [3]. Isolates required 7 days of incubation under an aerob conditiom in 35-37oC (but this organism was not strickly an aerob) [4]. The physiological microenvironment of the follicle and the microenvironmental adaptation of P acnes might been important factor in the penetration of this non motile bacterium into the follicle duct [4]. They grew optimum at 30-37oC (temperature in the follicle) [4].

The environment of the bacteria was probably more important than their absolute number for development of acne lesion [3]. In vitro, it had been shown that low oxygen tension, acidic pH (3,6-6,7) and nutrient supply [nitrogen, carbon, hydrogen, carbohydrate, amino acid, minerals, vitamin (biotin, nicotinic acid and thiamin)] markedly affected the growth of P acnes and the bacterial of active substances production such as lipase, proteases,hyaluronate lyase, phosphatase and smooth muscle contracting substance [3,4].

In the presence of light at high oxygen concentrations, P acnes grew well, but later the growth was inhibited because of photodamaging reactions involving excess oxygen and the endogenous microbial porphyrins [3].

The development of acne vulgaris was likely linked with the P acnes and very occasionally with the transient flora that were involved in acne (The transient flora was gram negative bacteria that was shed from anterior nares onto the adjacent skin after the resident flora was supressed by long term systemic or topical antibiotics) [3,4]. The limitted species of organism (resident organism) colonized the skin surface, such as propionibacteria, staphylococci, aerobic coryneform bacteria and the yeast Malassezia furfur [4].

Some microorganisms were appeared and dissapeared from the skin environment and constitued transient flora [4].

Inflamation processes

Cunlife reported that hystologically CD4+ T lymphocytes were found in eatly 6 hours papular acne inflammation, CD4+ T lymphocytes and neutrophyl were found in 24-48 hours, CD4+ T lymphocytes, macrophage and giant cells were found in 72 hours [4].

The dermal inflammation was not been caused by bacteria in the dermis. It was probably resulted from biologically active mediators (IL 1α, IL β, TNFα, etc) that diffused from the follicle where they were produced by the binding of bacterials to TLR2 receptor (or others) of monocytes, sebocytes, keratinocytes, perifollicular and peribulbar macrophages, langerhans cells and other immune cells or CD4+ of T lymphocytes [4,6,9,10]. There was an ability of innate immune system to use TLR2 receptor to recognonized microbial pattern and initiated immune response in cutaneous disease [9]. TLR 2 receptor induced inflammatory response and the development of antigen spesific adaptive immunity [6].

Pro inflammatory cytokine stimulated abnormal keratinocyte proliferation,differentiation and hypercornification that revealed obstructions, than there were follicles impaction and distention that formed comedos [2,3,9]. As the retained cells blocked the follicular opening, the lower portion of the follicle was dilated by entrapped sebum. Disruption of the follicular epithelium permitted the discharged of the follicular dermis [2]. The combination of keratin, sebum and microorganism led to pro inflammatory mediators releasing and lymphocytes, neutrophyls and foreign body giant cells accumulating [2]. In the early inflammation, inflammation was due to pro inflammatory mediators that moved through the duct wall into the dermis, and had not been caused by the duct ruptured [3]. Interleukine1α was a dominant proinflamatory cytokine that played role in comedonal acne vulgaris inflammation process [4]. Other pro inflamatory cytokines that were produced were IL6, IL8, IL12, IL4, IL10, TNFα [4].

Some kind of pro inflammatory cytokines that were produced by innate immunity in acne vulgaris in some journals were:

- TLR 2 receptor of the monocytes bound to P acnes to produce IL12, IL8 pro inflammatory cytokine [10].
- NLRP3 inflammasome of the human sebocytes and monocytes as mediated pathway bound to live P acnes in the sebaceous glands through caspase 1 expression & activation to produce IL1β [11,12].
- TLR 2 receptor of the keratinocytes bound to P acnes to produce IL8, human defensin 2 pro inflammatory cytokine [10].
- TLR2 receptor of human keratinocytes bound to P acnes through PAMPs-Pathogen Associated Mollecular Paterns to produce IL1α in 7 days of exposures that induced comedogenesis [13]. PAMPs were such as peptidiglycan (PG) and lipopolysacharida (LP) of P acnes [6].
- PAR 2 of the keratinocytes bound to P acnes to produce IL 1α, IL8, TNFα [10].
- TLR2 receptor of human monocytes and skin surface macrophages in human pilosebceous bound to microbial agent (P acnes, gram positive coccus) through NFkB/ Nuclear Factor kappa light chain enhancer of activated B cells activation and MAPK (Mitogen Activated protein Kinase) cascade to sinthesize and release of IL12, IL8. TNFα, IL1β [6,14].
- TLR 2 receptor of monocytes bound to gram positive coccus to produce IL12 [14].
- Monocytes bound to P ovale (lived or heat killed, opsonized P ovale through alternative complement activation pathway more stimulated than non-opsonized) to produce IL8, IL1α [15].
- Monocytes bound to gram positive bacteria to produce TNFα, IL6 [15].
- Monocytes bound to Gram negative bacteria bound to produce TNFα. IL1. IL6 [15].

IL 8 induced chemotactic factors might played an important role in attracted neutrophyl to the pilosebaceous unit that led to release lysosomal enzime that led to rupture follicular epithelium and further inflammation [14]. Furthermore, P acnes released lipases, proteases, hyaluronidase which contributed to tissue injury [14].

IL 8 induced chemotaxis and activation of neutrophyl and T cells [15].

IL12 promoted development of Th1 mediated immune response. And overproduction of Th1 cytokine such as IL 12 was implicated in the development of tissue injury in a certain autoimmune and inflammatory disease [14].

IL1α was low activated by lymphocytes, chemotaxis, activation of neutrophyl than induced inflammation [15]. Therefore, interaction of P ovale and phagocytic cells might serve to amplify the inflammatory response and encourage further recruitment of phagocytic cells [15]. P ovale upregulated phagocytic cells (macrophages) thus provided enhancer protection to bacterial and tumor cells [15]. There were down regulated of pro inflammatory cytokine with removed lipid [15]. Langerhans/ macrophages were able to take up antigen (acted as antigen presenting cells/APC) and then were presented to T cells [15].

P acnes activated monocytes cytokine relased through the pattern recognition receptors (PPRs), for example TLR2 receptor of the innate immune system [14]. So TLR 2 receptor was PPRs [14]. TLR2 receptor activation contributed to the pathogenesis of acne, suggesting that these cells promoted inflammatory responses at the site of the disease activity and induced pro inflammatory cytokine production [14]. Release of pro inflammatory cytokines that were mediated through TLR2 receptor had harmful effect in acne by promoting inflammation and tisuue destruction [14]. So TLR 2 receptor was a logical target for therapeutic intervention to block inflammatory cytokine response in acne and other inflammation condition which tissue injury was detrimental to the host [14]. Isotretinoin down regulated TLR2 that induced cytokine response [6].

Infestation of the organism itself was not the main cause of the disease but was rather caused by the various inflammatory responses that were initiated by microbial agents that led to destruction of the host tissue. Such responses were: the formation of immune complex, the recruitment and activation of neutrophyl and monocytes, the released of cytokines, released of dependent enzymes [14].

P ovale had 2 phenotypes, immunostimulated and immunosupressed phenotypes, P ovale (through an alternative pathway of complement activation) activated cellular immune response and humoral immune response [15]. Complement was the part of immune system that enhanced the ability of antibodies and phagocytic cells to clear microbes and damage cells from an organism, promoted inflammation and attacked the pathogen plasma membrane. It was part of innate immune system (which was not adaptable and did not change over the course of individual`s lifetime) and it could be recruitted by the adaptive immune system to finish the action. There were 2 complement activation: classical pathway (that was mediated by immune complex) and altenative pathway (that was mediated by yeast or bacterial cells) [15]. There was complement activation that involed in the early to later stages of inflammation and P acnes were capable for triggering both the alternative and classical complement pathways [1,3,4,15]. Complement activation caused lysis bacteria and virus, opsonization, inflammation [15]. In the early non inflamed and inflammed lession had shown that there was activation of the classical and alternative pathways [3]. And there were the type 4 immunological reaction to a non spesific antigens in the prior of obvious duct ruptured [3].

The majority comedones clearly represented a dermal pool of pro inflammatory IL 1α [4]. Spongiosis of the pilosebaceous follicle wall was the feature of early inflammation changed; this could lead to leakage of comedonal IL 1α into the epidermis [4]. The consequence was the activation of dermal microvascular endhothelial cells, selective accumulation of antigen non spesific to mononuclear cells and inititation of antigen independent cutaneous inflammation that consistent with the hystological features of early inflammation in acne [4].

In the later, in the moderate and severe inflammation, there was disruption of the duct and macrophage giant cell foreign body reaction [3]. An amplification phase via antigen dependent T cell responses to other comedonal components for example P acnes, might then developed [4]. The intensity and duration of the subsequent cell mediated response would been depended on many factors, including the degree of individual sensitization to their cutaneous microflora [4]. Following the disruption of cell wall, neutrophyl would been attracted into the duct by microbial chemotactic factor, that was proved by a study that demonstrated the capability of P acnes to attract neutrophyl in vitro [4]. So, P acnes might cause inflammation because this organism had been shown to secrete chemotactic factors and the chemotactic activity had been shown in comedones [1]. Low mollecular weight chemotactic factor did not require serum complement for activation and because of its small size, it could probably be escaped from follicle and attracted polymorphonuclear leukocytes [1]. If polymorphonuclear leukocytes enter the follicle, they could ingest P acnes organisms, resulted the release of hydrolytic anzymes which in turn, might been importance in producing follicular epithelial damage [1]. Polymorphonuclear leukocyte ingested P acnes were anti P acnes dependent antibody (ADCC) [1].

Bacterial cell walls fractions of P acnes were a potent chemoattractan for polymorphonuclear and mononuclear cells, could also produce prostaglandine like substance, that acted as non streroidal anti-inflammatory drugs, that had small anti acne effect [3].

It was likely but was not been proven that P acnes played an important role in acne inflammation [4]. Whether P acnes played a role in the initiation of inflammation in acne was questionable since it had not been colonized at all of the early lessions. Nevertheless, there was an increasing in the number of lessions colonized by P acnes following early inflammatory change. P acnes were a potent adjuvant that induced a chronic inflammatory tissue response because it was resistant to phagocyte killing and degradation [4]. So, P acnes caused chronic inflammation process because of its resistance to phagocyte cell and could not been degraded [4].

In the late phase of inflammation, P acnes dependent T cell lymphocyte response could be found, there were variations in Cell Mediated Immune Response depended on individual microflora sensitization [1,4]. Circulating antibody to P acnes were elevated in patient with severe acne [1]. Patients with severe acne were significantly more sensitized to P acnes than normal individuals, and the overall immunological status of patients were elevated compared with acne free individuals of the same age [4]. But this observation did not provide direct evidence for

a pathogenic role of P acnes in initiating inflammatory acne and might merely reflected an increased exposure of patient to the organism as result of their condition and might played a role in the exacerbation of chronic inflammatory response [4].

Lipid that got into dermis when the duct ruptured acted as an irritant and some lipids like linoleic acid could down regulated neutrophyl oxygen metabolism and phagocytosis, and contributed inflammation [3]. Inflammation was resulted from the production of free fatty acid and it showed that P acnes was the main source of follicular lipase that hydrolized trigliserida to free fatty acid [1]. The sebolemmal sheath accumulated inspisated sebum and formed a firm calculus which eroded the duct wall and contributed to inflammation [3].

DHT was the main driver of androgen induced sebum production of the skin. DHEA was another hormone for increasing sebaceous gland activity. Increasing DHEA secreted in adrenarche (puberty) could increase sebum synthesis. Sebum rich environment made skin P acnes grew and caused inflammation around follicle due to activation of innate immune system that increased pro inflammatory cytokines IL1α, IL8, TNFα, LTB4 production, then cytokines attracted various immune cells to the hair follicles (neutrophyls, macrophages, Th1 cells). IL 1α stimulated and triggered keratinocytes activity and reproduction which turned fueled comedo development [16].

P acnes provoked inflammation by altering sebum fatty composition [16].

P acnes oxydated squalene that

- Activated NFkB and consequently increased IL 1α levels.
- Increased 5 lipooxygenase enzym that responsible in arachidonic acid pathway- leukotriene B4 (LTB4) that promoted skin inflammation by acting on peroxisome proliferator activated receptorα (PPARα). PPARα increased activity of activator protein (AP1) and NFkB led to recruitment of inflammatory cells. AP 1 inflammatory cascade led activation of matrix metalloproteinase which contributed to local tissue destruction and scar formation [13].

2. P acnes Hydrolized triglycerides to pro inflammatory free fatty acid through lypase enzyme of P acnes. FFA spur production of antimicrobial peptides/AMPs (Such as Human β defensin 1/HBD1, cathelicidine, human β defensin 2/HBD2) thus leading to further inflammation.

That inflammation in acne lession was broken in the deep layer and formed nodules,in study was reported the elevated IgE levels that related with clinical severity in a group, but another group was found no changed in total IgE levels [3]. Female had better defence mechanism than male against P acnes [3,16]. Most acne patient had no misfit immunological reaction [3]. There were no circulating immune complexes in acne sera patients [3]. Skin testing with heat killed suspensies of P acnes demonstrated that subject with severe acne produced a greater inflammatory reaction at 48 h than other subject, suggested that host response might been important [3]. Changing in neutrophyl chemotaxis might been the secondary event [3]. P acnes polypeptide was detected in serum of the acne patients but were not in normal individu [3]. Acne fulminant showed exaggerated delayed hypersensitivity reaction to P acnes [3].

Affected & Predisposed Factor

Several factors that affected, predisposed, triggered, influenced, exacerbated or aggravated acne vulgaris were: genetic, racial, atopic, seborhoeic, mestruation, hormonal misfit, diet, environment. ultraviolet light, hot and humidity, sweating, friction, occupation, stress, cosmetic, pomade genetic. There were multifactorial genetical background and familial predisposition that had been proved in twin study [1,3,4]. Acne was polymorphous dermatosis with a polygenetic background, that did not follow Mendelian rules [4]. Most individual with cystic acne had parents with a hystory of severe acne [1]. Several studies had shown that genetic factor influenced susceptibility to acne [3]. There were 45% acne parents`s in schoolboys acne patient in Germany and were also supported by genetic study in twins [3,4,]. Besides genetic factor, the exogenous factor also influenced the severity of disease inflammation process, for example bacterial colonization [4]. Severe acne might be associated with XYY syndrome (rare) [1].

Racial: Acne in Black Americans were less evident than white Americans. Americans had more severe acne than Japanese [3]. Acne vulgaris was lower incidence in Asians and Africans [1].

Atopic: There was decreased incidence of acne vulgaris in atopic dermatitis patients that had low sebum production [3].

Seborrhoeic: Seborrhoeic dermatitis was concomitantly found with acne vulgaris in some cases, but the relationship had not been known [1].

Menstruation: About 70% patient reported 2-7 days premenstrual flared up of acne vulgaris related to sebaceous pores size changing that influenced the hydration of pilocebaceous epithelium [3,4]. There was an alteration of progesterone and estrogen levels [3,4]. Estrogen therapy increased SHBG and reduced free testosterone so there were decreasing of sebum production and libido [17].

The orifice of pilosebaceous duct was smallest between days 16-20 of the menstrual cycle. It reduced the flowed of sebum, produced relative obstruction and so increased the possibility of pro inflammatory cytokine mediators to concentrate in the lumen of sebaceous glands duct, thus stimulated the flare of acne premenstrually [4]. There was premenstrual changing in hydration of pilosebaceous epithelium and variation in sebum excretion during premenstrual cycle that flared acne [3].

Testosterone was produced by ovarium and adrenal gonad, testosterone than converted to estrogen and progesterone [17]. Testosterone levels peaked at the middle of menses phase (was around of ovulation) and there was increased libido [17]. Testosterone was converted to DHT by 5α reductase enzyme. Testosterone and DHT were androgen that stimulated and were binded to androgen receptor in the sebaceous gland thus stimulated sebum production [17]. Most of acne female had normal menstrual cycle and normal hormonal level [4].

Hormonal misfit: In 24% acne vulgaris patient had no hormonal abnormality [3]. Most acne patients had normal hormone levels

or levels at the upper end of normal range [3]. Most acne patients had no hormonal misfit, and had no need to investigate the hormonal problems in female patient [4].

Active sebaceous glands were required for the development of acne vulgaris [3]. Sebaceous activity was predominantly depended on androgen of gonadal and adrenal origin [3]. In the normal level of androgen production, there were increasing stimulation of sebum production in sebaceous gland of acne vulgaris patient [1]. There was also a possibility of an end organ hyper response of the pilosebaceous glands to normal circulating levels of androgen hormones [1,4]. And it was supported by the finding that the sebaceous glands in acne prone areas function differently to those in non-prone areas, so acne could be found only on the trunk and none on the face, or acne just on the face and none on the back and chest [4]. Acne vulgaris patient extended on average more sebum than normal subject, the level of secretion was correlated with the severity of acne [3]. Androgen hormone had pro inflammatory effect, so androgen levels and antiandrogen therapy influenced acne inflammation severity [4].

There were rare cases with excessive androgen production of ovarium, adrenal and pituitary that were found in some exceptional case like acne in children (5-7 years), individual who poorly responded to 3 course oral isotretinoin acne therapy, patient with clinical skin androgenic manifestations like excessive hair, hoarse voice, irreguler menstruation, could not got on well with the men, could not been pregnant and female pattern alopecia (in polycystic ovarian syndrome and congenital adrenal hyperplasia) [4].

Diets: Cunliffe said that overall dietary factor did not cause acne [4]. In study proved no correlation between acne severity and whatever food ingestion [4]. In personal study there were no link between acne severity, calory intake, carbohydrate, lipids, protein, minerals, amino acid and vitamin [4].

But the possible effect of nutrition on the age of puberty might been relevant, as acne was more likely occured after the starter of sexual development and this occured when the body weight attained about 48 kg [3].

The insidens of acne was low in people who had eaten rich fish diets and that was markly increased acne insidens in people who had eaten western diet with saturated fat [3]. It could be due to genetic factor [4].

Environmental factor also influenced the kind of people diet [3]. Chocholates, caramels and fatty acids were accused of aggravating acne [4]. High glycemic diets aggravated acne [2]. Chocholate had insuline like substance [2]. In high insulin levels, there were low SHBG levels and high free testosterone levels that increased sebum production. Insulin might affect SHBG, thereby influencing androgen clearance [3]. There was an inverse relationship between the serum levels of insulin and SHBG in woman [17]. In obesity there was raised insulin levels, lower SHBG levels & total testosterone in both sexes [14]. Lower SHBG resulted in increasing of free testosterone, the effect of high free testosterone levels resulted masculinization and high sebum production. Estrogen therapy increased SHBG and reduced free testosterone so there were decreasing of sebum production and libido [17]. However, post meal transient hyperinsulinemia did not play a role in hyperandrogenaemic acne patients [3]. And in study, high chocholate diet did not modulate the natural course of acne [4]. Chocholate appeared to have no significant influence in acne course study [3].

Reduced skimmed milk diet with calsium and vitamin D suplementation were benefit in acne patient and obesity [2].

Continuous low calori intake such as in anorexia nervosa patient and in patient with crash diet might improve the disease, and there were reducing of sebum excretion rate, changing sebum composition, decreasing sex hormones such as DHEA that explained clinical improvement of acne [4]. Dietary restriction resulted a mark weight loss and reduced seborhoea, but it could not be considered as routine treatment for acne [3]. Crash diets that were combined with strong physical stress could increase androgen release [4].

Environment: Acne insidence increased in people who migrated from east to western countries because of the dietary changing (rich fish diet to saturated fat diet), due to environment factor that influenced the people diet [4].

UV radiation: UV radiation was known to have wide ranging effect on cellular immunological system, but controled study on the therapetic effects were lacking [4]. UVA could convert squalene into squalene peroxidase which could enhanced comedogenesis but the other UV radiation like UVB, visible light (blue and red) and natural light 400-450 wavelength were beneficial to improve acne lesion [4]. Artificial UV radiation appeared to be less satisfactory than natural radiation [3]. UVB produced tanning of the skin that produced camouflage that led to a subjective improvement of acne [4]. Erythemathous and suberythemathous dose of UVB could led to scalling of the interfollicular epidermis and might helped corneocyte desquamated from around of acroinfundibulum [4]. Narrow band UVB particularly helped in eczema and psoriasis [4]. The wavelength 400-450 nm could activate porphyrins (in the bacteria) that were produced by P acnes and could helped to destroy P acnes in the acne follicles themselves [4]. Visible light in both red and blue light range had been shown to improve acne as effective as benzoil peroxide. It was suggested that red light was antimicrobial [4]. Photodynamic therapy was under invenstigation [4].

Sweating: Up to 15% patient noticed that sweating caused a deterioration in their acne, especially if they lived or worked in a hot humid environment, for example as a cook. Ductal hydration might be a responsible factor [3].

Hot and Humidity: Acne could be worsened dramatically if patients were exposed to tropical and subtropical climates [4]. The holiday to humid environment frequently precipitated acne [4]. It might relate to increase poral occlusive effect of skin hydration [4]. Excess humidity aggravated acne by an effect on sebum outflow [4].

Friction: Friction might contribute additional acne by irritating the upper parts of pilosebaceous duct [4].

Occupation: Hydration of the ductal stratum corneum induced acne in such occupation like catering [4]. Acneiform oil folliculitis and chloracne were the occupational acne [4].

Stress: It was unlikely that stress alone induced the formation of acne lesion [4]. However, acne itself induced stress and picking of the spot would aggravate the appearance [4]. That was particularly obvious in young females who presented acne excoriee [4]. Questionaire study had shown that many patients experience shame (70%), embarrassment and anxiety (63%), lack of confidence (67%), impaired social contact (57%) and significant problem with unemployment4 Severe acne might been related to increase anger and anxiety [4]. There were psychological and social effect of acne in inducing anxiety, depression and impaired the quality of life [4].

Cosmetic: It had shown that some cosmetic contained lanolin, petrolatum, certain vegetables oil, butylstearate, lauryl alkohol, oleic acid, isopropyl myristate, propylene glycol, D and C red dyes were comedogenic [3].

Pomade: Pomades were comedogenic greasy preparation [3].

Course & Prognosis

Acne vulgaris frequently cleared spontaneously by the early twentieth but could persisted to the fourth decade or older [1]. Treatment for acne might only require for 3-4 years, but the many patients with obvious clinical acne therapy would require for 8-12 years until the acne went into spontaneous remission [4]. Spontaneous remission frequently was around the age of 25 years, 93% of acne cases were resolved within 25 years and in 7% acne could persisted well into the mid-forties or early fifties (up to the age of 45 years) and they were called as mature acne [4].

Inflammed lessions developed dynamically, with the majority exhibiting polymorphic clinical and hystological appearance before resolving [4]. Papule might become pustular before resolving, ussually through the macular phase [4]. Over 50% of superficial lessions were resolved within 7-10 days, whereas the deep-seated nodules and pustules might persist for 10-30 days or even longer [4]. The lessions would been healed and exacerbated by many factors and made acne vulgaris as one of the chronic pilosebacebaceous diseases [3].

Flares occured in winter and with the onset of menses [1]. Several factors that affected, predisposed, triggered, influenced, exacerbated or aggravated acne vulgaris were genetic, racial, atopic, seborhoeic, mestruation, hormonal misfit, diet, environment. ultraviolet light, heat and humidity, sweating, friction, occupation, stress, cosmetic, pomade [4].

The squele of acne was scarring that might been avoided by early treatment, espescially with oral isotretinoin early in the course of the disease [1]. Early recognition and treatment of acne were important to prevent physical scarring espescially in inflammatory acne that could cause many psychological distresses [4].

Limitted studies suggested that resolution did not relate to reduction of sebum production or surface bacteria [3]. Pierard had shown that there was an individual sebaceous glands function at different rates in acne patients [3]. The resolution associated with spesific changed in these acne prone hypersecreting glands [3]. The relationship between ductal hypercornification, inflammatory mediators, changed in the host response and resolution was obscured [3].

Complication

Acne scars were acne vulgaris complication event with the excellent treatment available were performed [2]. Intense inflammation led scar formation [1]. Scars were frequentlly occured in cystic acne, but less severe lessions also formed scar [2]. There were 2 sorts of scarring [3,4].

1. There was loss of scar tissue (ice pick scar, depressed scar, macular atrophic scar, perifollicular elastolysis)
2. There was an increase of collagen tissue (hypertrophic scar, keloid scar)

Pitted scars/ice pick scars were typically occured on the cheeks. Perifollicular elastolysis was predominantly occured on the back, chest, neck. Keloid could be seen along the jawline and chest [2,4].

Scar might improve spontaneously over 1 year or longer [3]. The rare scars complications were Calsifications [3]. Other complications from acne were [3]:

- Prominent residual hyperpigmentation which was especially happened in darker skinned patients
- Pyogenic granuloma formation which was more common in acne fulminans and in patients treated with high doses isotretinoin
- Osteoma cutis which was consisted of small-firm-papules resulting from long standing acne vulgaris
- Solid facial oedeme, which was a persistent form facial swelling that was an uncommon but distressing result of acne vulgaris or acne rosasea.

Antibiotics resistances were the commonest complication. It was due to prolong treatment of acne vulgaris that was needed because of the disease chronicity [3,4]. Given treatment combination, changed the dose and duration of antibiotic therapy, given oral isotretinoin and the other non-antibiotics regimen could solve the resistances to antibiotic problems [3].

The rare long-term treatment of acne with antibiotics complication was gram negative folliculitis [3].

The lession appeared on anterior nares and extended to adjancent skin [1]. The physician should change the diagnosed if there were suddenly appeared pustules and nodules [1].

There 2 kinds of gram-negative folliculitis lessions were [2]:

1. Multipel pustules that were based on wide inflammation areas. It was more frequent. The etiology was Enterobacter and Klebsilla.
2. Deep indolent nodules. The etiology was Proteus.

Bacterial cultures and sensitivity tests should be performed to decide the prompt treatment. Ampicillin and trimetoprim were the treatment of choice for gram negative folliculitis. Oral isotretinoin was choosen for the resistent antibiotics cases [2,3].

Differential Dignosis

The differentials diagnosis of acne vulgaris were acneiform dermatosis, acne steroid, drug induced acne, acne aestivalis, acne agminata, acne varioliformis, adenoma sebaceum, boils, dental sinus, human immunodeficiency virus, folliculitis (Staphylococcus aureus folliculitis, Staphylococcus epidermidis folliculitis, demodex folliculitis, fungal folliculitis, Pityrosporum folliculitis), milia molluscum contagiosum, perioral dermatitis, plane warts, rosacea, seborrhoeic dermatitis, sycosis barbae, syringoma, trichoepitheliomata [1,4].

The differential diagnosis of acne scars was hidroavacciniforme, ulerythema ophryogenes, atrophia maculosa varioliformis cutis, porphiria cutanea tarda [4].

Treatment

Goal of therapy: The goal of therapy was: removed plugging of the pilar drainage, reduced sebum production, treated bacterial colonization and prevented from scarring [1,4]. The treatment might be required for 3-4 years, patient with obvious clinical acne required 8-12 years therapy until the spontaneous remission was occured. Spontaneous remission wouldl been occured in 25 years old and 7% could persisted until mid-forties-early fifties and were called as mature acne [3,4]. Early recognition and treatment of acne was important to prevent acne scarring that caused physiological distress [4].

Treatment modality: The treatment modality was:

1. Topical therapy: topical antibiotics (Erytromycin, clindamycin), benzoil peroxide, sulphur, resorcinol, salisilic acid, retinoic,azeleic acid
2. Oral therapy: oral antibiotics (doxycycline, tetracyclne, minocycline, amoxycillin, erytromycin, clindamycin, sulfa, dapsone), oral isotretinoin [1-4].
3. Physical therapy: intralessional triamcinolone acetonide, cryotherapy, comedo extraction, cauterry, chemical peeling, photodynamic terapy, excision, surgical for severe and resistant cases [1-3].
4. Hormonal therapy had good result in normal or abnormal laboratory test patient. Spironolactone and cyproterone acetate treated acne vulgaris by reducing sebum production, reducing androgen excess and alleviating cystic acne [3,4]. Other hormonal therapy reduced sebum production by reducing testosteron level, but clinically had serious side effect (finasteride, flutamide, estrogen, gonadotropine releasing agonist and metformin). TNF inhibitor (etanercept etc) [2].

Treatment of complication: The complications were acne scar, persistent hyperpigmentation, pyogenic granuloma formation, persistent form facial swelling and could been treated by laser, chemical peeling, skin needling and rolling, dermabrasion, laser dermablation, cryopeeling, filler, punch graft, intralessional steroid and fluorouracil [3].

The rare long-term treatment of acne with antibiotics complication was gram negative folliculitis [3].

Ampicillin and trimetoprim were the treatment of choice. Oral isotretinoin was choosen for the antibiotic resistance cases [2,3].

Chemical Peeling

Chemical peeling was one of the treatments of choice for acne and acne scar [17,18]. Chemical peeling/chemical resurfacing/ chemoexfoliation/chemosurgery involved an application of one or more exfoliating agents to the skin, resulting in the destruction of portion of the epidermis and/or dermis with subsequent regeneration. This produced controling wound and reepithelialization [19].

Acne vulgaris might been improved by superficial peeling, although medium peeling could aggravate or actually produced acne [19]. In rosasea the existing erythema of the disease made medium peeling riskier because of persistent tenderness or erythema [19]. Chemical peeling generally treated superficial acne scar [4]. Medium depth peeling with solid CO2 to efface the rims or the edge of depressed scar, was combined with immediate repetitive application of 35-50% TCA to the rims, had resulted in substantial improvement [19].

Chemical peeling could be used to improve the appearance of aging, wrinkled or sun damaged skin [17]. It was less effective in dealing with acne scars but it was a valid dermatological manouvre for these and the other superficial lessions on the face [17]. Chemical face peeling was given to conjunction with or as an alternative to dermabrasion. There were many protocols involved in different combination of chemical peeling; some were given in combination with laser dermablation [4].

A variety of preparation on differing concentration could been given alone or in combination, depending on the desired outcome [17]. Peels were categorized by the level of injury they caused [17].

Chemical peeling wounding classification, divided into 3 types [18,19]:

1. Superficial peeling wounding-to stratum granulosum/ papillary dermis
   a. Very light-stratum corneum exfoliation or stratum ghranulosum depth (α hydroxy acid, salisilic acid, TCA 10-25%, resorsinol, jessner`s solution, solid carbondioxide, tretinoin),
   b. Light-basal layer or upper papillary dermal depth (35% TCA unoccluded, single or multiple application)
2. Medium depth peeling wounding-through the papillary dermis to upper reticular dermis
   a. Combination peels, single or multiple applications (CO2+TCA35%, Jessner`s solutions+TCA 35%, Glycolic acid +TCA35%, 50% TCA unoccluded single applications)
   b. Full strengthth (phenol 99% unoccluded).
3. Deep depth peeling wounding to the mid reticular dermis (Baker Gordon, baker phenol croton oil unoccluded and occluded).

Patients with dry skin and fair complexion were the best subjects [17]. Fitzpatrick`s classification measured pigmentary responsiveness of the skin to ultraviolet light most often based on ethnic background. Skin type I-III were ideal for peeling, types IV-VI could also be peeled with all peeling agent but the risk of unwanted pigmentation was greater [19]. The neck should only be included with caution as the skin in this area was more prone to scars and hyperpigmentations [17]. Weaker

preparation was generally applied on eyelids and the care should not been taken to cause hypertrophic scars, which might occured around the mouth or mandible [17]. Prolonged erythema and increased sensitivity to sunlight and pigmentary changed (both hyperpigmentation and hypopigmentation) might followed the procedure [17].

In acne vulgaris, chemical peeling had keratolytic effect by dissolved intercellular cement and reduced corneocyte adhesion, anti-inflammatory effect by commedolytic action (Salisilic Acid was better) and bactericidal action (Glycolic acid was better) [20].

Peeling in acne: Chemical peeling was given as an adjunct to medical therapy in acne, because it produced complimentary rapid therapeutic effect and improvement in skin appearance and texture [21]. Primary effect was in comedone with a concomitant reduction in inflammatory lessions. Peels allowed topical agent to penetrate more efficiently into the skin and might improve PIH [21]. Peeling agent for acne: SA, GA, LHA, Jessner`s, TCA [17,21].

Peeling for post acne hyperpigmentation and rejuvenation: Chemical peels were evidence based in treatment of post acne pigmented macules and atrophic scars as they improved coexisting comedonal and papular acne, reduced post acne erythema and have a lightening effect on pigmentation at the base of healed lessions and scars [22]. Chemical peeling improved the depth contour and caused softening associated scars by their action on collagen remodelling and stimulation of new collagen activity [22]. All peels also added improvement in texture glow [22]. Chemical peeling also acted as priming for treatment of pigmented acne marks in skin of colors before resurfacing therapies with lasers and lights were sought for [22]. Chemical peeling was thinning the stratum corneum and regenerating a compact epidermis which reflected light evenly acrossed the skin surface and imparted a textural improvement and lightening effect by the elimination of epidermal melanin and prevention of transfer of melanin to keratinocytes [22]. Chemical peeling was resultant improvement in dyschromias, texture and fine lines. And rejuvenation effect was enhanced if the patients was well primed espescially in dark skin types [22].

Priming: Daily application of 0,1% tretinoin for 2 weeks prior to 35% TCA peels significantly enhanced the healing time of the facial, forearm and hand skin in a double-blind placebo-controlled study [19]. However, tretinoin application before and after TCA did not significantly enhance the clinical efficacy of the peel [19]. Topical tretinoin all trans retinoic acid was a suplement to most peel regimens along daily application of sunscreen [19].

Contraindication of chemical peeling: Those patients who were not closely cooperating with physician should not been treated [4]. There was evidence that patients should been off oral isotretioin for 1 year. Frequently relapsing herpes simplex was a relative contraindication [4]. Occasionally herpes simplex infection was an absolut contraindication and acyclovir prophylactic could been prescribed [4]. Peeling should not normally be performed during the sunny time of the year, because of the greater possibility to produce hyperpigmentation post therapy [4-17].

Complication of chemical peeling: Pigmentary changed in the form of hyperpigmentatiom might occured in darker skin types and was caused by sunlight, estrogens, photosensitizing drugs or pregnancy. Baker gordon depth peels could made hypopimentation and scarring. TCA 50% was capable of unpredictable hypertrophic scarring and hypopigmentation. Bacterial, fungal, viral infection might occur after peeling. Prolong erythema might occur after peeling and might been treated with topical hydrocortisone. Redness occured in patient who took alcohol beverages, suffered from contact dermatitis and took isotretinoin prior peel. Textural skin changed and the form of large pore occured temporarily after peeling. Skin atrophy, cardiac arythmia, laryngeal oedeme, exacerbation of koebnerizing pemphigus like disease might occured in phenol/croton oil peels [19].

Wound Healing in Chemical Peeling

Chemical peeling produced controling wound and reepithelialization [19]. Angiogenesis neovascularization, collagen deposition, re-epithelialization and tissue-collagen remodeling/maturation after skin wound/exfoliation that was provoked by chemical peeling would promote skin rejuvenation and regeneration, increased skin elasticity, improved texture glow and skin lightening.

Chemical peeling improved the depth contour and caused softening associated scars by their action on collagen remodelling and stimulation of new collagen activity. All peels also added improvement in texture glow. Chemical peeling was thinning the stratum corneum and regenerating a compact epidermis which reflected light evenly acrossed the skin surface and imparted a textural improvement and lightening effect by the elimination of epidermal melanin and prevention of transfer of melanin to keratinocytes [22].

Wound healing refered to a living organisms' replacement of destroyed or damaged tissue by newly produced tissue. A skin wound resulted from the breakdown of epidermal layer integrity. The wound healing began immediately after an injury to epidermal layer. The dynamic process included the highly organized cellular, humoral and molecular mechanisms [23]. Wound generally heal in 4 to 6 weeks. Wound healing, as a normal biological process in the human body, was achieved through four precisely and highly programmed phases: hemostasis, inflammation, proliferation (tissue growth), tissue remodeling (maturation and cell differentiation). For a wound to heal successfully, all four phases must occur in the proper sequence and time frame. Any disruption led to abnormal wound healing [24,25]. The events of each phase must happen in a precise a regulated manner. Interuption, aberrancies or prolongation in the process lead to delayed wound healing.

Wound healing occasionally classified as primary healing and secondary healing. Uncomplicated healing of a non-infected, well approximated wound was defined as primary healing. If the wound healing course of this wound was disrupted by infection, dehiscence, ischemia/hypoxia, reperfusion injury, collagen synthesis defect and immune disfunction, secondary healing stages began. It took years to heal. Secondary healing was most susceptible to infection resulted poor healing.

Many factors that impaired wound healing were resulted from systemic illness, such as diabetes, smoking, malnutrition. Local factors that impaired wound healing were pressure, tissue oedeme, hypoxia, ibfection, maceration and dehydration [23].

Wound healing was a natural physiological reaction to tissue injury. Wound healing was not a simple phenomenon but involved a complex interplay between numerous cell types, cytokine, mediators, and vascular system. The cascade of initial vasoconstriction of blood vessels and platelet aggregation was designed to stop bleeding. This was followed by an influx of variety inflammatory cells, starting with white blood cell. White blood cell, in turn released a variety of mediators and cytokines to promote angiogenesis, thrombosis and reepithelialization. The fibroblast in turn produced extracellular component and collagen formation. Fibroblast produced collagen as well as glycosaminoglycans and proteoglycans, which were major extracellular matrix component and the wound finally enter remodeling phase [24,25].

Homeostasis Phase

When injury occurred, the initial phase was always an outpouring of lymphatic fluid and blood. It was during this process that adequate homeostasis was achieved. Both extrinsic and intrinsic coagulation pathway were activated. Aggregation of platelets followed arterial vasoconstriction to the damaged endhothelial lining, A release of Adenosine Di Phosphate (ADP) resulted in clumping of platelets and initiated the process of thrombosis. This vasoconstriction was the short live processed that was soon followed by vasodilatation, which allow more white blood cell and thrombocytes [24,25].

Inflammatory phase

The inflammatory phase was characterized by homeostasis, chemotaxis and increased vascular permeability, limiting further damage, closing the wound, removing cellular debris and bacteria (Phagocytosis by white blood cells), and fostering cellular migration.

Neutrophyls and thrombocytes speed up inflammatory process by releasing more mediators and cytokines. Mediators like serotonin and histamine were realeased from platelets and increased cellular permeability. Inflammatory phase took several days [24,25].

Proliferation Phase / Growth of New Tissue

About 2-3 days after the wound occurred, fibroblast began to enter the wound site, marking the onset of proliferative phase even before the inflammatory phase was ended.

As in another phase of wound healing, steps in the proliferative phase did not occur in a series but rather partially overlap in time. This phase could last for several weeks [24,25].

The proliferative phase was characterized by angiogenesis/ neovascularization, collagen deposition, granulation tissue formation, re-epithelialization and wound contraction.

In angiogenesis, vascular endothelial cells form new blood vessels/vasculogenesis. Neovascularization occurred forming new blood vessels, which was the formation of new vessels from endhothelial progenitor cells.

In fibroplasia and granulation tissue formation, fibroblast grow and form new provisional extra cellular matrix (ECM) by excreting collagen. The platelets Derived Growth Factor (PDGF) attracted fibroblast and along with Transforming Growth Factor (TGF), enhanced the division and multiplication of fibroblast, then fibroblast in turn synthetized collagen. Besided the PDGF, other factors promoted collagen degradation, the transformation of fibroblasts, the growth of new vessels and reepithelialization. All the process occurred at the same time but in syncrhorized fashion [26].

Reepithelialization started and occurred with migration of cell from the wound periphery and adjacent edges. Initially only a thin superficial layer of epithelial cells was led down. Epithelial cell proliferated and crawl a top the wound bed, providing cover of a new tissue.

Tissue Remodelling /Maturation

By days 5 through 7 the fibroblast had started to lay down new collagen and glycosaminoglycans. These proteoglycans formed the core of the wound and help stabilized wound. Once collagen fibers had been led down on the fibrin framework, the wound started to mature. The wound also began continuing deposition of fibroblast and myofibroblasts. During maturation and remodeling, collagen was realigned along tension lines, and cell that no longer needed were removed by programme cell death (apoptosis) [24,25].

When the level of collagen production and degradation were equalized the maturation phase of tissue repair was said to had begun. During maturation, type III collagen, which was prevalent during proliferation was replaced by type I collagen. Originally disorganized collagen fibers were rearranged, cross linked and aligned along tension lines.

The onset of maturation phase was varied extensively dependening on the size on the wound and whether it was initially closed or left opened, ranging for approximately 3 days to 3 weeks. It could last for year or longer (in wound infection).

The maturation and remodeling phase was where the wound achieve maximum strength as it matures. It started week 3 to 12 months [24,25].

Skin Acidity in Acne Vulgaris

Skin pH was normally acidic, ranging between 4 - 6, while internal environment of the body maintains in a neutral pH to slightly alkaline (about 7,4). pH increased with each deeper corneocyte layer. The accidification of the skin surface was necessary for antibacterial activity, barier function, and maturation and structural integrity of the stratum corneum [33,34].

The acidic nature of whole skin surface was first claimed by Heuss in 1892. But the first scientific study relating to skin surface pH appears to had been carried out by Schade and Marchionini in 1928, who called it as the `acidic mantle. Eccrine sweat coat containing lactic acid was thought to be the major determinant of acidic pH of the stratum corneum previously. Hydrolysis of epidermal phospholipids and other complex lipids formed free fatty acid in the late stages of differentiation, also played an important role in accidification of the skin surface. Lipase activity

of resident bacterial flora and sebaceous glands also produce free fatty acids that accumulate on the skin surface, contributing to acidity. Urocanic acid generated from histidine metabolism might add significantly to acidic pool. Active energy requiring pathways like the sodium/hydrogen antiporter system influences the skin pH by regulating the hydrogen ion concentration. Skin surface pH was a parameter that cumulatively represented fhe function of various units of skin including stratum corneum [33].

Dark skin people had more acidic skin than white skin. Man had more acidic skin than woman. Skin pH influenced by skin product (cosmetics and cleanser) and diet.

Acidic pH of stratum corneum was essential for optimal functioning of the natural barier system of the skin. A shift in normal skin pH and barrier disfunction caused by irritan product predisposed the skin to several inflammatory acne vulgaris [34].

Epidermal keratinization involved the formation and recycling of an effective barier strata made of protein rich corneocytes and lipid rich cementing substance. The psocess required several enzymes that were pH dependent β glukocerebrosodase and acidic sphingomyelinase were involved in ceramide synthesis and required a pH of 5,6 and 4,5. Formation and processing of lamelar structures in the epidermis occured in an acidic environment. A transient increased in pH toward neutrality was linked to activation of serine proteases, involved physiologic desquamation by degradation of desmoglein 1. A sustained serine protease activity, because of persistently elevated pH inhibited lamelar body secretion and stimulated epidermal hyperproliferation. Follicular parakeratosis seen in acne prone areas accured secondary to epidermal hyperplasia could be potential consequence of the ranged pH [33,34].

The benefits of acidifying skin surface in acne or lowering skin pH reduced the inflammaory TH2 response and quickened barier function recovery and decreased Trans Epidermal Water Loss. Acidic pH preventing to epidermal proliferation.

The sign and symptom of skin irritation and the occurence of inflammatory lessions of acne were found to be lower in using acidic soap than alkaline soap. The phenomena of acidifying skin surface reduced the number of inflammatory papulopustules in affected acne skin. Lipid added to acid cleaser reduced the interaction between surfactant and skin lipids, and partialy replaced the skin lipid barier that removed by washing [33]. Rendon et al, reported that β lipohydroxy acid (LHA), a derivate of salicylic acid reverted keratinization of pilosebaceous unit in acne to normal skin turnover. By the virtue of its pH 5,5 being similar to normal skin, it cleany detached individual corneocytes rather than uneven exfoliation of the cells in clumps as seen with salicylic acid and glycolic peels [35].

In study in Indian adult population that measures facial skin pH found that the mean pH value in the healthy control group was within the normal range for the stratum corneum. The sex difference in PH that observed in both control and acne groups was insignificant. Increased skin pH was a significant feature in acne patients compared with the control. In study showed that the skin of patients with acne was chronically in state of stratum corneum instabillity, which could explain the underlying pathology. This was simply represented by increased skin pH at basal conditions. Since skin pH was a multifaceted index that was influenced by various factors, its distict role in acne pathogenesis was often overlooked. In systematic review of literature, there was evident that increased/disturbed of startum corneum pH could be a pivotal role ti occurence and recurence of acne [33].

Epidermal Barrier in Acne Vulgaris

Acne Vulgaris was associated with inherent abnormalities in epidermal barier function. Acne skin had higher Trans epidermal water loss (TEWL) and sebum secretion and lower stratum corneum hydration, that affected acne degree severity. The increase in TEWL was observed to show more severe in acne skin patient.

The balance of skin hydration and sebum production was also thought to influence comedogenesis. Skin with less than 10% moistured content could result in impaired stratum corneum and inflammatory cytokine production. Therefore, adequate skin water content (10-20%) was essential in acne vulgaris prevention [31,32].

In acne skin patient there were lower ammounts of sphingolipids (ceramides and free sphingosine) that observed corresponding with diminished Water Barier Function (WBF) that showed as increased of TEWL So decreased ammount of free sphingosine and total ceramides which was indicated to a deficient intercellular lipid membrane and correlated with impaired Water Barier Function, then accompanied by hyperkeratosis follicular, that was all responsible in comedo formation [31,32].

Alteration in follicular keratinization were integral component of acne pathogenesis. Fillagrin was the key protein in epidermal differentiation and contributed to the structural and functional integrity of the skin. Within acne lessions, there was an increase in fillagrin expression in keratinocytes lining the follicle wall, that caused by P. Acnes. Reduced ability to express fillagrin correlated directly with the lesser ability to form acne lession [31].

Topical therapies for acne such as benzoil peroxides, retinoids, antibiotics with alcohol-based preparation and acid preparation caused skin irritation and lack of patient's adherence. Dryness or skin irritation caused barier disruption of stratum corneum leading to increased TEWL and production of inflammation.

It recommeded to use moisturizer as adjunctive treatment of acne to fix skin irritation caused by topical acne therapy. Moisturizer contributed independently to improve signs and symptom of acne. Moisturizer was consisted of three main properties which were occlusive, humectant and emolient effects. The occlusive ingredient was physically blocked TEWL by forming a hydrophobic film on the skin surface and within the superficial interstitium between corneocytes. Humectant was atracted water from the dermis to epidermis. Emmolient was smooth skin by filling space between skin flakes with a drop of oil [33-35].

Moisturizer increased skin hydration and decreased Trans Epidermal Water Loss that were higher in acne skin patient. Adding moisturizer application had been shown to have good efficacy in acne management [33].

Some medication for acne such as peeling caused alteration and disrupted integrity and function and caused skin irritation. Providing spesific skin care recomendation, proper consultation and product selection, proper use topical medication and choose moisturizer as adjuvant treatment to minimize skin irritation was the important part in acne management.

Peeling Agent

Chemical peeling was a methods of targeted cutaneous ablation using specific caustic agents that allowed for rapid predictable and uniform thickness of chemoablation to a desired cutaneous depth, ultimately resulting in improved appearance of the skin. Chemical peels were the third most commonly performed noninvasive cosmetic procedure in US, with over 1.300.000 procedures performed in 2016 alone. There has been a paradigm shift in the recent years with laser largely sup [lanting deep peels. Despite this shift, superficial peels had proliferatived in both popularity and product diversity [27].

When used in appropriate indication and with the proper technique, nearly all the peeling agents had demonstrated excellent clinical safety and efficacy. It remained and indispemsable cost-effective tool for dermatologists.

TCA

TCA was probably the most commonly applied agent [17]. Weak preparation 10-15% might been applied for light freshening peels and higher concentrations for medium depth or deep peels [17]. The depth of injury was depended on acid concentration and the number of applications. Need no neutralization [17]. TCA 10% was superficial chemical peeling, considered as adjunctive therapy in acne, often added to the first line therapy such as retinoids and antibiotic, and as the first line therapy for acne scar and skin rejuvenation [19]. In high concentration was good for treating acne scar (CROSS/Chemical Reconstruction of Skin Scars technique) [4,19]. TCA was cheap and save because no systemic absorbtion, but it felt pain (more than SA,less severe than phenol) [19].

TCA was an effective haemostatic caustic, which had many uses [17]. The 30-50% concentration could be given as styptic and was frequently employed as conjunction with superficial curretage in the treatment of solar keratosis, seborrhoeic warts, etc [17]. The supersaturated solution could be applied on its own to treat many benign and dysplastic skin lession [17].

TCA was useful treatment for xanthelasmata and solar lentigos [17]. It should be applied with great care, however, especially around the eyes [17]. Its action was rapid and white frosting occured within a few seconds of application [17]. The caustic action could be partially neutralized by applying alcohol, water or sodium bicarbonat soaked gauze but this was unlikely to have any effect once the acid had penetrated the skin [17].

Excess sebum should first be removed using detergent, ether or acetone [17]. TCA should then be applied with an almost dry applicator. The concentration that was applied could vary according to the site, the condition to be treated and whether the TCA was being applied as a styptic or a superficial skin caustic [3]. Weaker solution of TCA was sometimes given for treating wider areas of skin [17]. Because of deliquisence TCA should been kept in close, coloured and corrosion resistant bottle [17].

TCA 50% was similar to phenol in its destructive effect on the epidermis [17]. TCA chemical peeling caused epidermal coagulation and collagen necrosis up to the upper reticular dermis, reepithelialization begun from survival islets of keratinocytes and skin appendages and the clinical effects were due to resultant increased in dermal volume of collagen, glycosaminoglycans and elastin [17,19]. Keratolitic and comedolitic effect of TCA diminished free fatty acid that was important for bacterial and fungal growth, so it acted as antibiotic and antifungal adjuvant therapy and could solved resistance problems to antibiotic and antifungal in acne therapy.

α hydroxy acid (AHA, Lactic acid, glycolic acid, malic acid)

α hydroxy acid was mild [17]. α hydroxy acid for example glycolic acid could acted as superficial peels or freshening peels and at high concentration as medium depth chemical peels [17]. The depth of injury depends on pH, concentration of the acid, amount applied/layer and duration/length of treatment time [17]. Should been neutralized [17].

AHA chemical peeling therapy started with a 2 weeks course of 10-15% glycolic acid daily application, then increased application up to 20-35% weekly or every second week [4]. To induce better and deeper effects one had to use in concentration up to 70% [4]. The application time until the neutralization of the pH could also be increased [4]. The glycolic acid concentration, time of application and interval between therapies could be adapted to the patient`s individual needed, deeper effect could be obtained by 20% TCA in water, TCA concentration up to 45% were also in use [4].

GA could normalize keratinization and increase epidermal and dermal hyaluronic acid and collagen gene expression. GA 70% reduced comedo. In lower concentration GA improved both inflammation and non-inflammation lessions [21]. GA improved pigmentation and diminished acne flared after the first treatment [21]. Salycilic Acid (β hydroxy acid).

It had comedolytic and keratolytic effect. Need no neutralization [17]. Treated comedo and inflammation in acne, whereas SA was better than GA [21].

Jessners

Jessner`s solution was mild [17]. Jessner`s solution was contained of phenol, salicylic acid, lactic acid in ethanol. It was self-neutralizing; the depth penetrance was depended on times of applied/layer [17]. Jessner`s had significant greater degree of exfoliation and reduced sebum secretion, compared with GA.21.

Baker Gordon formula (88% phenol, crotton oil)

Phenol acted as deep peels [17]. Phenol had systemic absorbtion, the side effect was cardiac arytmia, nephrotoxic. Phenol caused complete coagulation of epidermal keratin protein that blocking further penetration. Croton oil had keratolytic effect and potentiated the depth penetration of phenol [17].

Superficial Peeling

Superficial peels caused wounding to the epidermis and might reach the papillary dermis (dermal epiderrmal interface) [17,21]. Superficial peeling agent induced increasing upper dermal collagen production in response to repeated epidermal

slough [19]. Superficial peels exerted their action by decreasing corneocytes adhesion and increasing dermal collagen [21]. These peels were good methods for rejuvenating the epidermis and upper dermal layers of the skin [21]. After superficial peels epidermal regeneration could been expected within 3 to 5 days and desquamated was frequently well accepted [21]. These peels were well tolerated by patients who required limitted down time after treatment [17]. Superficial peeling which was generally epidermal and pose little risk of scarring [19]. They could be used in all fitzpatrick`s skin types, skin colors and body areas [19].

Superficial peels were given in the treatment of photoaging, acne, actinic keratosis, solar lentigines and pigmentary dyschromias [17]. Given the limitted nature of the injury was induced by these peels, patients frequently needed multiple treatments on the weekly or monthly for effectiveness basis to reach a desired result [17,19]. They did not vesiculate and patient generally continue to normal activity [19]. Minimal post operative care was needed for superficial peels and patient might returned to their normal daily activity immediately, could appllied cosmetics to conceal erythema [19].

However, patients needed to be properly counceled regarding the limited benefit of superficial peels, which could not improve wrinkles and deep furrows that might been possible improved by deeper injury peels [17]. Repeated superficial peels could not produce the same result as a single deeper peel [17].

α hydroxy acids (AHA`s): Naturally occuring agents that were typically derived from foods, included glycolic acid (sugaracne) lactic acid (sour milk), malic acid (apples) and citric acid (citrus fruits). Glycolic acid had smallest moleculear size and thus greater bioavailibility that made it was the one of the most frequently applied AHAs [17]. The depth of injury was determined by the pH, concentration of the acid, amount applied and length of treatment time [17]. Glycolic acid in concentration up to 70% was frequently needed to applies for melasma, acne and photoaging [17]. Following rapid application to the entire face, it should be neutralized with sodium bicarbonat or plain water [17]. Glycolic acid had been given in combination with 5FU for the treatment of actinic keratosis [17].

Salicylic acid: Salicylic acid was β hydroxy acid, could been given in concentration of 20-30% for the treatment of acne and mild photoaging [17]. It was especially useful as an adjunctive treatment for acne because of both the keratolytic and the comedolytic properties of the salicylic acid [17]. It was also given in combination with other agents as part of Jessner`s solution [17]. Salicylic acid tended to be less inflammatory than other superficial chemical peels [17]. After application, patients experience some mild stinging and discomfort [17]. A whitening of the skin, was termed as frosting, from the precipitation of salicylic acid crystals was noted within several minutes of application [17]. Salicylic acid did not require neutralization, although cool compresses after application could sooth the skin [17].

Trichlor Acetic Acid: TCA in concentration at 10-25% was applied extensively as a superficial peel. The depth of injury was related to the concentration and the the number of applications, with repeated coats of a low concentration TCA leading to greater penetration [17]. The agent was applied, and erythema and a white frost were noted within 1 minute. Patients experienced a burning sensation [17]. Handheld faned and post procedural cool compreses could reduce discomfort [17]. TCA did not require neutralization after application [17]. TCA 10-35% needed to accomplish superficial peeling on facial and non-facial areas, such peel might be repeated every 7-28 days [19].

Jessner: Jessner`s solution was a combined of resorcinol, salicylic acid and lactic acid in ethanol [17]. This superficial peel had keratolytic activity and it was typically given for acne or hyperkeratotic lessions [17]. It was self-neutralizing and multiple application could be performed to obtain a deeper injury [17].

Solid CO2 (Dry ice): It had been given alone or in and combination with TCA to obtain a deeper peel [17]. It had been proposed as an effective treatment for acne scars and as a way to potentiate the effect of TCA to achieve a deeper peel [17].

Medium Depth Peeling

Medium depth chemical peeling was defined as a controlled wound through the epidermis and down to the deep papillary dermis [17]. In contrast to multiple treatments that were frequently performed with superficial peels, medium depth peels were generally done as single procedure because of the more significant injury produced and more robust clinical response [17]. These peels caused epidermal necrosis and dermal injury which resulted in increased collagen production during the wound healing process over the next several months [17]. Medium depth peels healing process was longer, with full epithelialization occuring in about 1 week [21]. Medium depth peeling might be repeated every 3 to 12 months based on the amount of active damage that remaining or reccuring after the peel on for continue scar effacement [19]. Medium depth peels were indicated for treatment of mild to moderate photodamaged, rhytids, pigmentary dyschromia, actinic keratosis, solar lentigines and other epidermal growth [17].

The medium depth peel was 50% TCA [17]. However, it was not generally applied currently as a single agent peel because of the unpredictable results and increased incidence of scarring and dyspigmentation (hypopigmentation) [17,19]. Rather combining 35% TCA with an initial application of another agent, such as solid CO2, jessner`s solution or glycolic acid could produce a medium depth injury (equal with 50% TCA) without the complications associated with higher concentrations of TCA alone [18,19]. As the result of the damage to the epidermis produced with the initial peel, the lower strength TCA was able to penetrate deeper and produced a more significant and even result [17]. Side effect of medium depth peeling was hyperpigmentation espescially in dark skinned patients and sun protection was recommended for several weeks after treatment [21].

Deep Peeling

Deep chemical peels were defined as those that caused an injury down to the mid reticular dermis [17]. Deep peeling caused rapid denaturization of surface keratin and other proteins in dermis and outer dermis [21]. Penetrating into the reticular dermis, the deep peels maximized the generation of new collagen [21]. Epithelialization occured in 5 to 10 days, but deep peels required

significant healing time, ussually 2 months or more and sun protection should be given [21].

These peels were indicated for patients with moderate to severe photodamage and advanced rhytids [17]. Deep peels produced more significant injury and patients had to extended period of postoperative healing [17].

Baker Gordon formula phenol peel was the traditional deep peel [17]. Undilluted 88% phenol did not produce a deep or consistent injury because it caused complete coagulation of epidermal keratin proteins, thus blocking further penetration [17]. The Baker Gordon formula reduced the concentration of phenol to 55%, the croton oil acted as a keratolytic and potentiated the depth of penetration of the phenol [17]. Cardiac monitoring was required because phenol could produce arrythmias [17]. Intravenous fluids were given before and during the peel to limit the serum concentration of phenol and any potential renal complications [17]. In addition, the face was divided into smaller cosmetic units, which were treated individually [17]. A 15 minutes waiting was required between treating each subunit, spreading the entire procedure over 1-2 hours, thus further limitting the systemic concentration of phenol [17]. Following application, occlusive tape could be applied if deeper wound was desired [17]. The patients were managed conservatively in the postoperative period with petrolatum and wound care until the skin was healed [17]. In addition to the cardiac and systemic concerns assosiated with deep peels, other risk included hypopigmentation, textural abnormality and scarring [17]. If any of the phenol solution accidentally contacted with the eyes, mineral oil should be given to flush, because water could potentiate the effect of the phenol [17]. Antiviral prophylactic should be administered [17].

Aim of the Study

The general purpose of this study was to prove the effectivity of TCA 15% superficial chemical peeling for treating all of acne lessions type (comedos/non inflammed and papule-pustules/ inflammed) and total of acne lessions.

The spesific purposes of this study were:

1. To know `was there significant decreased of the amount of acne lessions/differences between before and after treatment with one layer of 15% TCA superficial chemical peeling that showed the effectivity of this treatment for comedos, papule-pustules and total acne vulgaris lessions`
2. To know `was there significant clinical improvement in Global Acne Grading System (GAGS) for acne Aseverity classification between before and after treatment with one layer of 15% TCA superficial chemical peelings that showed the effectivity of this treatment for comedos, papule-pustules and total acne vulgaris lessions`

Counted the amount of comedos and papule-putules lessions and classified of acne severity according to Global Acne Grading System before and after peeling to describe the effectivity of 15% TCA Superficial Chemmical Peeling. Acne severity classification was according to The Global Acne Grading System. Classification was performed to judge the grade and severity before and after treatment (in a Cohort experimental research design).

A quantitative descriptive and analitic/inferensial were the statistical analysis methods that were choosed to describe clinical improvement and the signifficant decreased of the amount of acne lessions and acne grading severity (scoring due to GAGS) before and after treatment.

Saphiro Wilk test was performed to know was the sample distribution came from normal population sample distribution or not, then it continued to parametric analitic statistical analizes paired t test if sample came from normal population distribution and continued to non-parametric analitic statistical analyzes Wilcoxon Sign Rank Sum Test if sample came from non-normal population distribution.

Materials and Methods

- Patient informed concent
- Complete data and quesioner to find trigger and predisposition factor
- Counting acne lessions and group the types of lessions to comedos, papule and pustules. Then Classified the severity of acne lession according to The Global Acne Grading System for acne classification before and after peeling
- Taking Photograph before peeling and 14 days after peeling
- One layer of 15% TCA superficial chemical peeling was applied on the face following Rubin Technique chemical peeling procedures. Patient was lying down on the peeling bed. Both of the eyes were covered with kassas. Then 15% of TCA peeling was applied one layer using brush, firstly on the forehead, both of the cheeks, chin and nose. To faster frosting and minimize pain, cool compress and fanning were applied and moisturizing cream was applied after peeling.

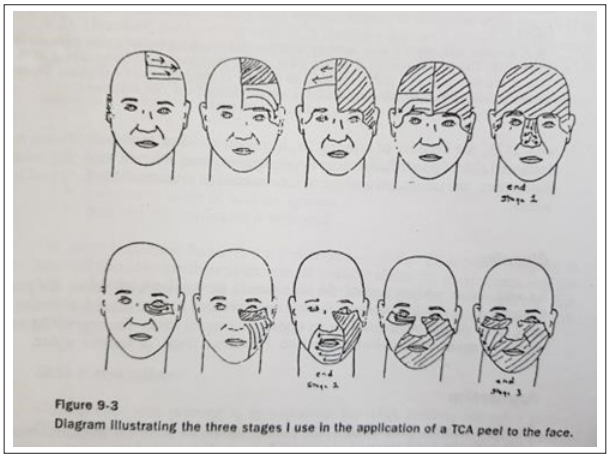


Figure 1: Rubin Technique for peeling

- The evaluation of acne grading severity was judged according to The Global Acne Grading System for acne classification before and after peeling treatment, The severity was judged by scoring the calculation of factor x grade.
- The evaluation of clinical improvement/difference of acne before and after treatment was judged by counting the difference the all of type of acne lession and the difference of GAGS score.

Table 1: The global acne grading system[23]

Location	Factor
Forehead	2
Left cheek	2
Chin	1
Right cheek	2
Nose	1
Chest and upper back	3

Calculation: Each type of lesion is given a value depending on severity: no lesions=0, comedones=1, papules=2, pustules=3 and nodules=4. The score for each area (local score) is calculated using the formula: Local score=Factor×grade (0-4). The global score is the sum of local scores and acne severity was graded using the global score. A score of 1-18 is considered mild, 19-30, moderate; 31-38, severe; and>39, very severe

Figure 2:
Research Design and Statistical Analysis
Samples : Total sampling

Inclusion criteria:
1. All patients who had acne lessions on the face (comedos and papule-pustules).
2. The age > 14 years old 3. Agree to join research.

Had no other acne treatment

Exclusion Criteria
1. Patients with the hystory of oral Herpes simplex or other skin diseases on the face.
2. Got Isotretinoid in the last 6 month.
3. Pregnant.
4. Got laser, dermabration, filler or botox treatment before

Place : At outpatient clinic.
Time : 6 months
Research Design: Cohort experimental study.
Statistical Analysis:
1. Quantitative/Descriptive (charts)
2. Qualitative/Analitic

Saphiro Wilk Normality Test then continued to Pairet t test for normal sample distribution or WilcoxonSign Rank Sum Test for non-normal sample distribution

Photograph Evaluation
Photograph before peeling and after peeling

Result
In this research 14 patients 93% of samples were woman, at the age between 15-23 years old. The mean of the age was 18,78 (95% CI 17,10 - 20,46) ± 2,81 years. Most samples at the age of 16 years old (36%)., The longer for the Length of the sickness of the samples was less than 1 year (64 %). The mean of length of the sickness was 1,71 years (95% CI 1.05 to 2,37) ± 1.09 years Genetic factor was positive as predisposition factor in 85,7% of samples.

Nobody had acne that was triggered by chemical product. Cosmetic/make up was triggered factor in 42,9 % of samples. Stress was triggered factor in 28,6 % of samples. All of samples was at the normal cycle of menstruation and menstruation was as triggered factor of acne in 92,3 % of samples. Diet was triggered factor in 35,7% of samples.

According to Global Acne Grading Severity System of acne classification, the acne severity before peeling samples in this research were grouped to mild 57,14%, moderate 14,18%, severe 28,57% and no very severe acne vulgaris. The result of acne grading severity after peeling therapy were good, no acne 28,57% and mild 71,4%, no severe or very severe acne.

The grade of acne according to Global Acne Grading System before peeling was 100% at the 3rd grade, and the grade of acne after peeling were 35,7% was at the 0 grade (no acne), 21,4% was at the 1st grade, and 42,9% was at the 2nd grade of acne and nobody was at the 3rd and 4th of acne.

The mean of Acne Score according to Global Acne Grading System before peeling was 16,78 (95%CI 10,61 to 22,95) ± 10,3. The mean of Acne score according to Global Acne Grading System after peeling was 3,71 (95% CI 1,72 to 5,7) ± 3,32. The mean of difference of acne score before-after peeling was 13,07 (95% CI 7,78 to 18,36) ± 8,82.The mean of difference percentage of acne score before-after peelings was 74,15% (95% CI 58,57% to 89,73%) ± 26,001%.

There was significant decreased in acne grading severity, that was described in graph/charts as decreased amount of comedos-papuleputules and total of acne lessions. Most of the total acne lessions of the samples were comedos: 1458 lessions (94,9%), total papule pustules were 78 (5,1%). After peeling total comedos count were 451(95,9%). Total papuloputules count after peeling were 19 (4,04%).

The mean of difference of papulepustules before-after peelings was 5,14 (95% CI 1,23 to 9,52) ± 6,52. The mean of percentage difference of papulepustules before-after peeling was 81,66% (95% CI 65% to 98,3%) ± 27,8%.

The mean of difference of comedos before-after peelings was 83,92 (95% CI 21,42 to 146,42) ± 94,18. The mean of percentage difference of comedos before-after peeling was 85,23% (95% CI 74,09% to 96,36%) ± 16,78%.

The mean of difference of total acne lessions before-after peelings was 77,07 (95% CI 22,49 to 131,65) ± 91,09. The mean of percentage difference of total acne lessions before-after peeling was 86,79% (95% CI 76,95% to 96,62%) ±16,41%.

The result of statistical analyzes using Wilcoxon Sign Rank Sum Test: there were significant difference before and after treatment in counting of acne lessions (comedos, papulopustules and Total types of acne) and in decreasing of acne score according to GAGS for classification of acne severity. It meant 15% of TCA Superficial Chemical peeling was good and effective to treat comedos, papulopustules and the total types of acne lessions.

Sample Description Sex
Fourteen samples were collected in this research, most of samples were women (93%).

Age: There were 14 samples collected in this research at the age between 15-23 years old. The mean of the age was 18,78 (95% CI 17,10 - 20,46) ± 2,81 years. Most samples were at the age of 16 years old (36%).

Length of Sickness
The longer of the Length of sickness of the samples was less than 1 year (64 %). The mean of length of the sickness was 1,71 years (95% CI 1.05 to 2,37) ± 1.09 years.

Genetic
In this research acne genetic factor was positive as predisposition factor in 85,7% of the samples.

Trigger factor
Cosmetic
In this research cosmetic was the triggered factor and induced acne lessions in 42,9% of the samples.

Stress
In this research stress was the triggered factor and induced acne lessions in 28,6 % of the samples.

Menstruation
In this research menstruation was the triggered factor and induced acne lessions in 92,3% of the female samples.

Diet
In this research diet was the triggered factor and induced acne lessions in 35,7% of the samples.

Descriptive and Analytic Statistical Analyzes

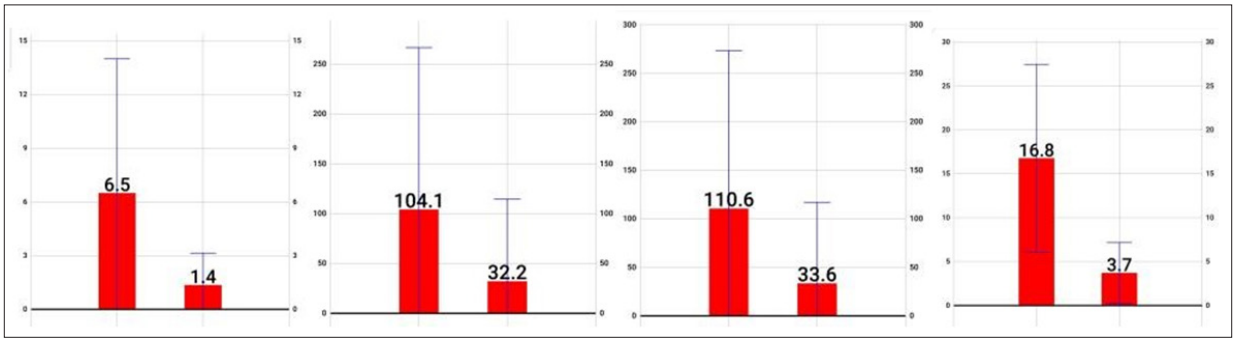


Figure 3:

The Mean of Papulopustules Before After Peeling
The mean of papulopustules before treatment was 6,5 (95% of CI 2,17 to 10,83). ± SD 7,50. The mean of papulopustules after treatment was 1.36 (95% of CI 0,33 to 2,39). ± SD 1,78

The Mean of Comedos Before After Peeling
The mean of comedos before treatment = 104,14 (95% of CI 10,35 to 197,94), ± SD 162,44. The mean of comedos after treatment = 32,21 (95% of CI -15,3 to 79,72). ± SD 82,28

The Mean of Total Acne Lessions Before After Peeling
The mean of total acne lession before treatment = 110,64 (95% of CI 16,63 to 204,66) ± SD 162,83. The mean of total of acne lession after treatment = 33,57 (95% of CI -14,61 to 81,75) ±SD 83,44.

The Mean of Gags Acne Score Before After Peeling
The mean of Acne Score according to Global Acne Grading System before peeling was 16,79 (95% of CI 10,61 to 22,96) ± 10,69. The mean of Acne score according to Global Acne Grading System after peeling was 3,71 (95% CI 1,72 to 5,71) ± 3,45.

The Differences of All Kind of Acne Before After Peeling
The mean of difference of papulepustules counts before-after peelings was 5,14 (95% CI 1,23 to 9,52) ± 6,52. The mean of difference of comedos count before-after peelings was 83,92 (95% CI 21,42 to 146,42) ± 94,18. The mean of difference of total acne lessions counts before-after peelings was 77,07 (95% CI 22,49 to 131,65) ± 91,09.

The mean of percentage of difference of papulepustules was 81,66% (95% CI 65% to 98,3%) ± 27,8%. The mean of percentage of difference of comedos was 85,23% (95% CI 74,09% to 96,36%) ± 16,78%. The mean of percentage of difference of total acne lessions was 86,79% (95% CI 76,95% to 96,62%) ±16,41%.

The Total Amount and Differences of All Kind of Acne Lessions Before-After Peeling
There was significant decreased in acne grading severity, that was described in graph/charts as decreased amount of comedos-papuleputules and total of acne lessions. Most of the acne lessions of the samples before peeling were comedos : 1458 lessions (94,9%) and total papule pustules were less 78 (5,1%). After peeling, the count of total comedos were 451 (95,9%). total papuloputules were 19 (4,04%).

The Difference of Gags Acne Score Before After Peeling
The mean of Acne Score according to Global Acne Grading System before peeling was 16,78 (95%CI 10,61 to 22,95) ± 10,3. The mean of Acne score according to Global Acne Grading System after peeling was 3,71 (95% CI 1,72 to 5,7) ± 3,32.

The mean of difference of GAGS acne score before-after peeling was 13,07 (95% CI 7,78 to 18,36) ± 8,82. The mean of difference percentage of acne score before-after peelings was 74,75% (95% CI 58,57% to 89,72%) ± 26,001%.

Classification of Acne Severity
Classifications of acne severity was according to Gobal Acne Grading System in acne grading severity classification before and after one layer of 15% TCA chemmical peeling therapy, according to Global Acne Grading System, the acne severity classification of the samples before peeling were grouped to mild 57,14%, moderate 14,18%, severe 28,57% and no very

severe acne vulgaris. The result of acne classification after peeling therapy were good, no acne 28,57%, mild 71,4% and no severe or very severe acne.

The grade of acne according to Global Acne Grading System before peeling was 100% at the 3rd grade, and the grade of acne after peeling were no acne 35,7%, 1st grade 21,4% and 2nd grade 42,9% and nobody was at the 3rd grade and 4th grade of acne.

Spss Kolmogorov Smirnov Normality Test

All of datas in this research (the count of comedos, the count of papulopustules, the count of total acne lession and GAGS Scores) were in normal distribution due to Kolmogorov Smirnov Normality Test. Research Data was ratio in normal distribution, but less than 30 samples, so it was continued to Wilcoxon Signed Rank Sum Test (Non parametric statistic) as Statistical Test to know the result of this research.

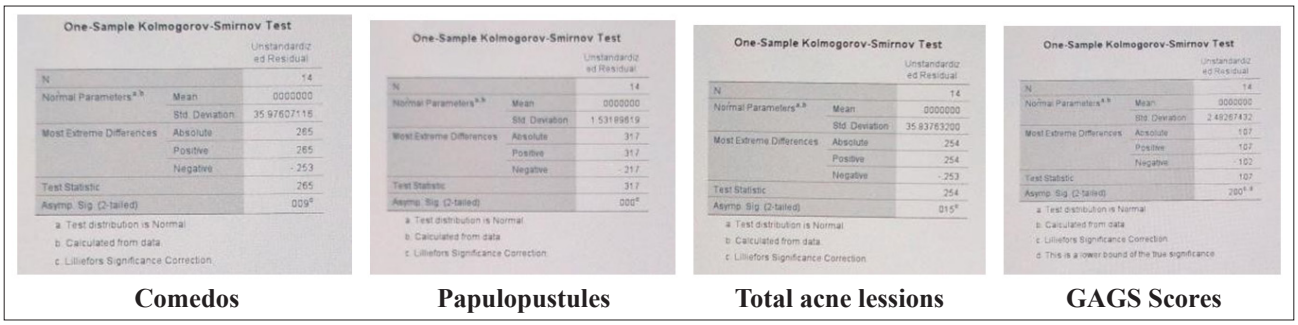


Figure 4:

Spss Wilcoxon Signed Rank Sum Test

Hipotesis:

Accepted H0: There was no difference before and after treatment

Accepted H1: There was significant difference before and after treatment

Spss Wilcoxon Signed Rank Sum Test for Comedos

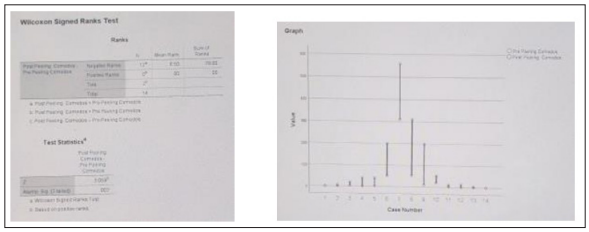


Figure 5:

The result of SPSS Statistical analysis for Comedos Before and After peelings:

- Negative ranks in total comedos count before and after peeling (decreased of the count of comedos) in 12 samples
- No positive ranks (No increased of the count of comedos before and after peelings)
- Ties (No difference count of comedos before and after peeling) in 2 samples (No comedos before and after peeling)

Wilcoxon Signed Ranks Statistical Test Asymp. Sig (2 tailed) is 0,002, less than 0,005. So Accepted H1, there was significant difference in decreased count of comedos before and after peeling.

Spss Wilcoxon Signed Rank Sum Test for Papulopustules

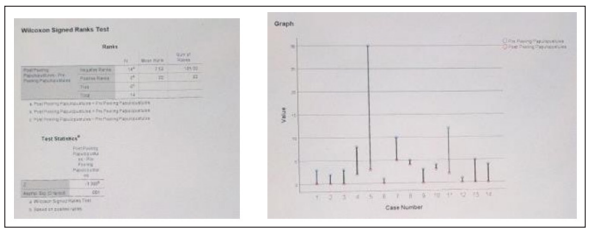


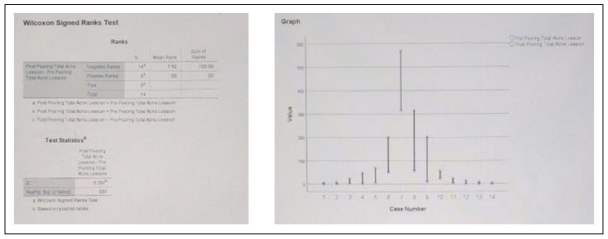
Figure 6:

The result of SPSS Statistical analysis for papulopustules Before and After peelings:

- Negative ranks in total papulopustulescount before and after peeling (decreased of the count of papulopustules) in 14 samples.
- No positive ranks and ties.

Wilcoxon Signed Ranks Statistical Test Asymp.Sig (2 tailed) is 0,001, less than 0,005. So Accepted H1, there was significant difference in decreased count of papulopustules before and after peeling

Spss Wilcoxon Signed Rank Sum Test for Total Acne Lesion



The result of SPSS Statistical analysis for Total Acne Lessions Before and After peelings:

- Negative ranks in total Acne Lessions before and after peeling (decreased of the count of total acne lessions) in 14 samples.
- No positive ranks and ties.

Wilcoxon Signed Ranks Statistical Test Asymp.Sig (2 tailed) is 0,001, less than 0,005. So Accepted H1,
there was significant difference in decreased count of total acne lessions before and after peeling

Spss Wilcoxon Signed Rank Sum Test for Gags Scores

The result of SPSS Statistical analysis for GAGS Scores Before and After peelings:

- Negative ranks in GAGS Scores before and after peeling (decreased of GAGS Scores).
- No positive ranks and ties.

Wilcoxon Signed Ranks Statistical Test Asymp.Sig (2 tailed) is 0,001, less than 0,005. So Accepted H1, there was significant difference in decreased of GAGS Scores before and after peeling.

Conclusion of statistical analysis
15% TCA superficial chemical peeling was effective to treat non inflammatory(comedos) acne lessions and inflammatory (papulepustules).

The conclusion of descriptive and analytic statistical analysis for samples description and triggered factor:
In this research 14 patients 93% of samples were woman, at the age between 15-23 years old. The mean of the age was 18,78 (95% CI 17,10 - 20,46) ± 2,81 years. Most samples were at the age of 16 years old (36%). The longer for the Length of the sickness of the samples was less than 1 year (64 %). The mean of length of the sickness was 1,71 years (95% CI 1.05 to 2,37) ± 1.09 years. Genetic factor was positive in 85,7% of samples.

Nobody had acne that was triggered by chemical product. Cosmetic/make up was triggered factor in 42,9 % of samples. Stress was triggered factor in 28,6% of samples. All of samples was at the normal cycle of menstruation and menstruation was as triggered factor of acne in 92,3 % of samples. Diet was triggered factor in 35,7% of samples.

The conclusion of descriptive and Analytic Statistical analysis for decreased acne lession count and the percentage of differences:
There was significant improvement before and after peeling with one layer of 15% TCA chemical peeling therapy, in acne grading severity, that was described in charts as decreased amount of comedos-papuleputules and total acne lessions. The mean of difference of GAGS acne score before-after peeling was 13,07 (**74,75%**). The mean of difference of papulepustules before-after peelings was 5,14 (**81,66%**), comedos was 83,92 (**85,23%**) total acne lessions was 77,07 (**86,79%**).

According to Global Acne Grading Severity System of acne classification, before peeling samples in this research were grouped to mild 57,14%, moderate 14,18%, severe 28,57% and no very severe acne vulgaris. The result of acne classification after peeling therapy were good, no acne in 28,57% of samples, mild in 71,4% of samples and no severe or very severe acne.

The grade of acne according to Global Acne Grading System before peeling was 100% at the 3rd grade, and the grade of acne after peeling were no acne 35,7%, 1st grade 21,4% and 2nd grade 42,9% nobody was at the 3rd grade and 4th grade of acne

The conclusion of analitic non-parametric statistical analysis Wilcoxon Sign Rank Sum Test:
There was significant difference of Clinical Improvement that showed as decreased of the total count of acne lession (comedo. papulopustules and total acne lessions) and decreased of GAGS score for acne grading severity before and after peeling with one layer of 15% TCA superficial Chemical Peeling.

Discussion
Sex: Fourteen samples were collected in this research, most of samples were woman (93%). Acne vulgaris was more complex and multifactorial in nature, reflecting the interplay of many factors such as increased access to proper health care, sosioeconomic status of individuals and family, and shifting cultural perceptions of skin and beauty, that made woman seek doctor to find proper health care more than man.

Woman was prone to acne. Imm other study, the prevalence of acne was higher in woman at the rate of 6,06% (95% CI, 5,99% - 6,12%), than in man at the rate of 3,34% (05% CI 5,99% - 6.12%). Male to female ratio of prevalence was around 1: 1,81. In each age category, women were at higer risk of developing acne than man [36].

Age: There were 14 samples collected in this research at the age between 15-23 years old. The mean of the age was 18,78 (95% CI 17,10 - 20,46) ± 2,81 years. Most samples were at the age of 16 year (36%).

In other study showed that girls aged 7-12 years old had the highest prevalence rate of acne at 17,78% (95% CI 17,42%-18,14%). The decreasing trend of acne prevalence in men was after the age 13 years. Women at high school age (13-18 years) remain at higher risk of developing acne, reaching prevalence at 14,15% (95% CI 13,85% - 14,46%) [36].

The Global Burden of Diseases Study proved that acne vulgaris affected 85% of young adult at the age 12-25 years [37]. In other literatures, the peak insidence of acne vulgaris was in 17-21 years, 17-18 years in female and 19-21 years in males. The age of onset was at puberty, typically 12-15 years, but could firstly appeared at 25 years old [4].

Length of the Sickness: The longer of the Length of sickness of the samples was less than 1 year (64 %). The mean of length of the sickness was 1,71 years (95% CI 1.05 to 2,37) ± 1.09 years.

The lessions would been healed and exacerbated by many triggered factors (menstruation, hormonal misfit, diet, environment. ultraviolet light, climmate, heat and humidity, sweating, friction, occupation, stress, cosmetic, pomade) and made aulcne vulgaris as one of the chronic pilosebacebaceous diseases. Inflammed lessions developed dynamically, with the majority exhibiting polymorphic clinical and hystological appearance before resolving. Papule might become pustular before resolving, ussually through the macular phase. Over 50% of superficial lessions were resolved within 7-10 days, whereas the deep-seated nodules and pustules might persist for 10-30 days or even longer.

Acne vulgaris frequently cleared spontaneously by the early twentieth but could persisted to the fourth decade or older. Treatment for acne might only require for 3-4 years, but the many patients with obvious clinical acne therapy would require for 8-12 years until the acne went into spontaneous remision. Spontaneous remission frequently was around the age of 25 years, 93% of acne cases were resolved within 25 years and in 7% acne could persisted well into the mid-forties or early fifties (up to the age of 45 years) and they were called as mature acne [4].

Genetic: In this research, genetic factor was acne predisposed factor in 85,7 % of samples.

There was multifactorial genetical background and familial predisposition that had been proved in some twin study, proved that acne had heritability of up to 80%. Acne was polymorphous dermatosis with a polygenetic background, that did not follow Mendelian rules. Several studies had shown that genetic factor influenced susceptibility to acne. Besides genetic factor, the exogenous factor also influenced the severity of disease inflammation process, for example bacterial colonization, menstruation, cosmetic and other acne trigger factors [1,3].

In study of Australian samples in 4.491 twins and their sibling aged from 10-24 years phenotypes analized that the polychoric correlation for monozygotic twins was higher (r = 0,86). Another twin's study revealed that heritability of acne on the back was very higher than dizygotic twins r = 0,42, 95% CI 0.35-0.47. Additive genetic aspect was responsible in genetic variance of acne severity and estimated heritability was 0,85 (95% CI 0,82-0,87) [38].

High heritability estimated for acne in twins were reported. In other twin study reported that heritability of acne on the back was very high. Higher correlation of sebum excretion and the proportion of branched fatty acids in the fraction of sebaceous wax esters was found in monozygotic vs dizygotic twins. A large twin studies reported that 81% of the variance of the disease was attributed to additive genetic effects, whereas remaining 19% was attributed to unique unshared environmental factors.

Remarkably at the age 14 years, facial acne in girls was less influenced by genetic factors than in boys and was significantly influenced by common environment factors [39,40].

Chromosomal abnormalities, HLA phenotypes and polymorphism of various genes had been associated with acne. Data from familial studies confirmed familial clustering. A family history of acne was associated with the earlier occurence of acne disease, increased number of retensional lessions, and therapeutic difficulties and relaps after oral isotretinoin treatment [39].

Acne Triggered Factors

Several factors believed as the aggravating factors of acne such as inn adequate face washing, hormone, sweet diets, greasy food, make up/cosmetic, washing/chemical product, stress, climmate, sweat, hot and humidity. A Cross-sectional study in Montenegrin Schoolchildren in 500 samples, acne was reported in 249 (49,8%) of samples aged 14-17 years. proved that acne improved in patient that diets changed to healthier food choices (77,4%), increased water consumptions (77,8%), cosmetic treatments (80,4%) and being on school holidays (62,2%) [41].

Chemical/Product: This research showed that no body applied chemmical/product that then triggered acne. In comprehensive systematic review 2005 there were sufficient evidence that facial cleansing or hygiene maintenance caused exacerbating or curing acne vulgaris in patients.42,43 Montenegrin Schoolchildren cross sectional in 500 samples of acne, washing was triggered factor in 85% of cases [41].

Acne patient tended to take self-treatment by excessive scrubbing or washing face that caused dryness or skin irritation and caused barier disruption of stratum corneum leading to increased and production of inflammation [29-37].

Acne Vulgaris itself was associated with inherent abnormalities in epidermal barier function. There were lower ammounts of sphingolipids (ceramides and free sphingosine) that observed corresponding with decreased Water Barier Function that showed as increased of TEWL Acne skin had higher TEWL and sebum secretion and lower stratum corneum hydration, then accompanied by hyperkeratosis follicular, were all responsible in comedo formation.

Cosmetic: In 42,9 % of the samples in this research, cosmetics acted as acne trigger factors. In A questionairs cross sectional analytical study in 149 girls in Sri Lanka showed cosmetic used in 90% samples and there was significant positive association between frequent exposured to cosmetics and severity of acne. Cosmetic usage was a potential aggravating factor that led to acne [42]. Montenegrin Schoolchildren cross sectional in 500 samples of acne, make up was triggered factor in 71,2% of cases [41].

It had shown that some cosmetic contained lanolin, petrolatum, certain vegetables oil, butylstearate, lauryl alkohol, oleic acid, isopropyl myristate, propylene glycol, D and C red dyes were comedogenic. Frequent use of lotion contains cocoa butter provoked comedogenic acne, but it improved skin tone and hyperpigmented scar. The long-term use of pomade (a mixture of petrolatum, lanolin and oil) as moisturizers for hair and scalp caused secondary acne errupting. Cosmetics occluded skin pores that caused comedos [41].

Stress: In this research 28,6 % of samples had stress as acne triggered factor. In questionnaires based cross sectinal study showed that anxiety was the acne exacerbating factor in acne. An interventional study found that patients had an improvement in their acne compared to control when receiving biofeedback training, relaxation training and stress reduction techniques [42,43]. In Australian study at the Melbourne University, stress was an exacerbating factor in 67% students and in Korean study acne was an exacerbating factor in 82% patients [44,45]. Montenegrin Schoolchildren cross sectional in 500 samples of acne, stress was triggered factor in 67,8% of cases [41].

In the National Health Insurance database, which included 98% of the population of Taiwan in 2006, identified that that were major depresion and suicide based on ICD 9 CM Codes in acne patients. Totally 47111 patirnts with acne were identified (16.568 males and 30542 females) from 1 million subjects. Major depression was more common in subjects with acne (0,77%) than controls (0,56%) $p < 0,0001$. The increased risk of major depression in women without acne was in Odds ratio 1,85% (95% CI 1,75%-1,96%). The risk was increased in women with acne at Odds Ratio 2,78% (85% CI 2,43% - 3,17%). Similar increased risk of suicide was noticed in women with acne. This study proved that acne and gender were associated with major deppression and suicide [36].

Strong systemic stress activated the hypothalamic pituitary adrenal (HPA) axis as the main adaptive response to stress, to produce CRH (Corticotropine Releasing Hormon). CRH acted as central coordinator for neuroendocrine and behavioral responses to stress. CRH stimulated sebaceous lipid gland production and steroigenesis that than converted to androgen resulted sebaceous gland hyperplasia and increased sebum production and inflammation which contributed to acne [46,47].

Peripheral nerves released the neuropeptide substance P or vaso intestinal peptide in response to stress. P substance stimulated the proliferation and differentiation of sebaceous glands and upregulated lipid synthesis in sebaceous cells. Physiological stress delayed wound healing up to 49% patients, so stress affected healing of acne lession [48,49].

Acne itself induced stress and picking of the spot would aggravate the appearance. Severe acne might be related to increase anger and anxiety. There were psychological and social effect of acne in inducing anxiety, depression and impaired the quality of life [48,49].

Menstruation/Hormonal: In this research menstruation was the provoked factor and induced acne lessions in 92,3 % of the samples.

In 24% acne vulgaris patient had no hormonal abnormality. Most of acne female had normal menstrual cycle [4]. In a questionaires multicenter epidemiological study in 1236 samples from 17 general hospital in Korea showed that menstruation aggravated acne [49]. Montenegrin Schoolchildren cross sectional in 500 samples of acne, menstruation/hormonal was triggered factor in 84% of cases [41].

In case control study in Menoufiya University Hospital of Egypt in 60 female patients with acne, there were increased total testosteron and free testosteron and lower SHBG in 42 patiens (70%) that statiscally had significant different than control, serum estradiol was lower in 45 patient (75%) of acne patients and had statistically significant different than control, serum progesterone was elevated in 40 acne patientns (66,6%) and statistically had significant difference than control [50].

Testosterone, DHT, DHEA were androgen that binded to androgen receptor in the sebaceous gland then stimulated sebum production caused acne. Testosterone was produced by ovarium and adrenal gonads, testosterone than converted to estrogen and progesterone. Testosterone levels peaked at the middle of menses phase (was around of ovulation). 5 α reductase enzyme in the infundibular sebocytes can convert testosteron to the more potent DHT.

Menstrual flare and increased sebum production also caused by progesterone which receptors were expressed at the basal epidermal keratinocytes only. Estrogen reduced sebaceous glands size so decreased sebum production, increased SHBG so decreased Free Testosteron, directly counteracted to testosterone action in sebocytes and influenced genetic regulation of sebaceous glands and sebocytes formation. Increased Insulin that caused by high glycemic diets inhibited SHBG so increased free testosteron and increased sebum production. CRH was secreted by hypothalamus targeted at sebaceous glands and induced lipogenesis by enhancing androgen bioavailibility and stimulating DHEA to potent testosterone [51].

Most of acne female had normal menstrual cycle and normal hormonal level. About 70% patient reported 2-7 days premenstrual flared up of acne vulgaris related to sebaceous pores size changing that influenced the hydration of pilocebaceous epithelium. There was an alteration of progesterone and estrogen levels. Estrogen therapy increased SHBG and reduced free testosterone so there were decreasing of sebum production [3,4].

The orifice of pilosebaceous duct was smallest between days 16-20 of the menstrual cycle. It reduced the flowed of sebum, produced relative obstruction and so increased the possibility of pro inflammatory cytokine mediators to concentrate in the lumen of sebaceous glands duct, thus stimulated the flare of acne premenstrually.There was premenstrual changing in hydration of pilosebaceous epithelium and variation in sebum excretion during premenstrual cycle that flared acne [3].

Diets: In this reseach food was provoked and aggravating acne in 35,7% patients. In cross sectional questionaires survey in Podgorica Montenegro in 500 samples, sweet food aggravated acne in 82% samples, greasy food aggravated acne in 72,6% samples [41]. But in some literature found that the insidens of acne was low in people who had eaten rich fish diets and that was markly increased acne insidens in people who had eaten western diet with saturated fat. Environmental factor also influenced the kind of people diet that caused acne. Chocholates, caramels and fatty acids, High glycemic diets were aggravated acne. Westerm diet was the diet that caused of increasing frequency of acnes. It was a dietary regimen characterized by high ammount of sugary desserts, refined grains, high protein, high fat dairy products and high sugar drinks, Western food was also common be found and became trending food in developing country. In US more than 80% fast food restaurant visitors were individual younger than 18 years old where acne was most common found [41]. But some studies found that overall dietary factor did not cause acne and proved no correlation between acne severity and whatever food ingestion. In personal study there were no link between acne severity, calory intake, carbohydrate, lipids, protein, minerals, amino acid and vitamin [4].

15% of Tca Superficial Chemmical Peeling to Treat Acne Vulgaris

In this research, the result of non-parametric statistical analyzes using Wilcoxon Sign Rank Sum Test was: there was significant difference in clinical improvement of acne counting lessions (comedos, papulopustules and total acne lessions) and decreasing of GAGS acne score before and after peeling treatment. It meant 15% of TCA Superficial Chemical peeling was good and effective to treat comedos, papulopustules and the total types of acne lessions,

There was significant improvement before and after peeling with one layer of 15% TCA chemical peeling therapy, in acne grading severity according to Global Acne Grading System and decreasing amount of comedos-papuleputules and total acne lessions, that was described in charts. The mean of difference of GAGS acne score before-after peeling was 13,07 (**74,75%**).

The mean of difference of papulepustules before-after peelings was 5,14 (**81,66%**), comedos was 83,92 (**85,23%**) total acne lessions was 77,07 (**86,79%**).

According to Global Acne Grading Severity System of acne classification, before peeling samples in this research were grouped to mild 57,14%, moderate 14,18%, severe 28,57% and no very severe acne vulgaris. The result of acne classification after peeling therapy were good, no acne in 28,57% of samples, mild in 71,4% of samples and no severe or very severe acne.

Chemical peeling was a methods of targeted cutaneous ablation using specific caustic agents that allowed for rapid predictable and uniform thickness of chemoablation to a desired cutaneous depth, ultimately resulting in improved appearance of the skin. Chemical peels were the third most commonly performed noninvasive cosmetic procedure. There has been a paradigm shift in the recent years with laser largely suplanting deep peels. Despite this shift, superficial peels had proliferatived in both popularity and product diversity. When used in appropriate indication and with the proper technique, nearly all the peeling agents had demonstrated excellent clinical safety and efficacy. It remained and indispensable cost-effective tool for dermatologists.

In Chengdu, China Study 2021 that compared 25% of TCA with 30% of Salicylic Acid chemical peeling in 20 samples every 2 weeks in four seasons showed that there was no significant difference in the effectivity between TCA and SA peels to treat mild to moderate acne vulgaris. TCA and SA in terms of the percentage of total improvement for all lessions (85% vs 95%, RR 0,89;95% CI 0,73-1.10), for non-inflammatory lession (80% vs 70%; RR 1.14; 95% CI 0,80-1,64) and the inflammatory lessions (80% vs 85%; RR 0,94; 95% CI 0,71-1,25). No adverse effect was identified for the SA peel, but in TCA peel was reported post inflammatory hyperpigmentation in 4 samples (20%) that lasted for 3-4 weeks [52].

Study in India showed that 25% TCA was comparable and showed no significant difference in the effectivity to 30% GA Peels to treat mild and moderate acne vulgaris, but safety and tolerability were better in SA than TCA peel. TCA peels was better in treating non inflammatpry lessions, while SA peels were better to treat inflammatory lessions [53].

Others Study in India 2015 showed that Jessner`s combined with 20% TCA peeling more effective to treat acne scar compared with 20% TCA Peeling alone. Marked improvement of acne scar after peeling in the first group was 60% versus 28% in second group [54].

Study In Chengdu, China Study 2021 also compared some other peeling agent and showed that SA 30% was more effective to treat non inflammatory and inflammatory acne vulgaris than Jessner sollution. Local side effect like initial burning sensation, postpeeling erythema and mild scalling were reported in both SA and Jessner peeling groups. Combination 20%SA and 10% Mandeic was superior than 35% GA peeling every 2 weeks in six sesions to treat comedos, papules and pustules. Comparison between GA & Amino Fruit Acid peels in the same concentration had same effectivity to treat all types of acne vulgaris. 30% GA & 50% Piruvic Acid Peels had same effectivity to treat all types of acne vulgaris. 30% GA compared with 30% SA peels showed that GA better decreased the number of acnes lession and patients preferred GA than SA [52]

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Many other studies of literatures reported the efficacy of chemical peeling to treat comedos and papulopustules acne vulgaris. And showed that there were no significant different in efficacy between any different peeling agent (SA 30% compared with GA 30-70%) [55].

In the retrospective Study of Nigerian in Port Harcourt, Nigeria in 27 patients had few side effects and effective. The comparison of treatment outcome on the clinical improvement by age, sex and category of chemical peels revealed no significant difference in clinical improvement. Minimal side effect (skin dryness and hyperpigmentation) was reported in 7,4% samples. The most common indication of peeling was acne vulgaris in 55,6% and melasma in 14,8% of samples [56].

In some other studies proved that TCA was slightly more effective (better/superior) than Salysilic acid to treat comedos. But in other research proved that no signifficant difference between TCA and Salysilic acid to treat comedonal acne. TCA treated inflammatory lessions/papule-pustules slightly less effective than Salysilic acid. Glycolic acid was superior than TCA and Salysilic acid to treat inflammatory acne lessions (papule-pustules).

Chemical peeling/chemical resurfacing/chemoexfoliation/ chemosurgery involved an application of one or more exfoliating agents to the skin, resulting in the destruction of portion of the epidermis and/or dermis with subsequent regeneration. This produced controling wound and reepithelialization.

Chemical peeling was given as main therapy or as an adjunct to medical therapy in acne, because it produced complimentary rapid therapeutic effect and improvement in skin appearance and texture. Primary effect was in comedone with a concomitant reduction in inflammatory lessions. Peels allowed topical agent to penetrate more efficiently into the skin and might improve PIH.

Chemical peels were evidence based in treatment of post acne pigmented macules and atrophic scars as they improved coexisting comedonal and papular acne, reduced post acne erythema and have a lightening effect on pigmentation at the base of healed lessions and scars. Chemical peeling improved the depth contour and caused softening associated scars by their action on collagen remodelling and stimulation of new collagen activity. All peels also added improvement in texture glow. Chemical peeling also acted as priming for treatment of pigmented acne marks in skin of colors before resurfacing therapies with lasers and lights were sought for. Chemical peeling was thinning the stratum corneum and regenerating a compact epidermis which reflected light evenly acrossed the skin surface and imparted a textural improvement and lightening effect by the elimination of epidermal melanin and prevention of transfer of melanin to keratinocytes. Chemical peeling was resultant improvement in dyschromias, texture and fine lines. And rejuvenation effect was enhanced if the patients was well primed espescially in dark skin types.

TCA in concentration at 10-25% was applied extensively as a superficial peel. The depth of injury was related to the concentration and the the number of applications, with repeated coats of a low concentration TCA leading to greater penetration. The depth of injury was depended on acid concentration and the number of applications.

The agent was applied, and erythema and a white frost were noted within 1 minute. Patients experienced a burning sensation. Handheld faned and post procedural cool compreses could reduce discomfort. TCA did not require neutralization after application.

TCA was probably the most commonly applied agent. Weak preparation 10-15% might been applied for light freshening peels and higher concentrations for medium depth or deep peels.

TCA Superficial peels were given in the treatment of photoaging, acne, actinic keratosis, solar lentigines and pigmentary dyschromias. Given the limitted nature of the injury was induced by these peels, patients frequently needed multiple treatments on the weekly or monthly for effectiveness basis to reach a desired result. They did not vesiculate and patient generally continue to normal activity. Minimal post operative care was needed for superficial peels and patient might returned to their normal daily activity immediately, could appllied cosmetics to conceal erythema.

TCA 15% was superficial chemical peeling, could be considered as the main therapy in acne, could be added to other acne therapies. It also could be chossen as the first line therapy for acne scar and skin rejuvenation. In high concentration was good for treating acne scar (CROSS/Chemical Reconstruction of Skin Scars technique). TCA was cheap and save because no systemic absorbtion, but it felt slightly pain in application (more pain than SA,less severe pain than phenol).

15 % TCA Superficial peels caused wounding to the epidermis and might reach the papillary dermis (dermal epiderrmal interface). TCA Superficial peeling agent induced increasing upper dermal collagen production in response to repeated epidermal slough. Superficial peels exerted their action by decreasing corneocytes adhesion and increasing new dermal collagen formation. These peels were good methods for rejuvenating the epidermis and upper dermal layers of the skin. After superficial peels epidermal regeneration could been expected within 3 to 5 days and desquamated was frequently well accepted. These peels were well tolerated by patients who required limitted down time after treatment. Superficial peeling which was generally epidermal and posed little risk of scarring. They could be used in all fitzpatrick`s skin types, skin colors and body areas.

The 15% TCA superficial chemical peeling was thinning the stratum corneum and regenerating a compact epidermis which reflected light evenly acrossed the skin surface and imparted a textural improvement and lightening effect by the elimination of epidermal melanin and prevention of transfer of melanin to keratinocytes. It increased angiogenesis/neovascularization, collagen deposition, re-epithelialization and tissue-collagen remodeling/maturation.TCA superficial chemical peeling promoted skin rejuvenation and regeneration, increased skin elasticity, improved texture glow and skin tightening and lightening. It improved dyschromias, texture and fine lines.

In superficial chemical peeling, fibroblasts proliferation produced new collagen and glycosaminoglycans, the proteoglycans, then it started to mature. During maturation and remodeling, collagen was realigned along tension lines, and cell that no longer needed were removed by programme cell death (apoptosis). The level of new collagen production and degradation were equalized and the maturation phase of tissue repair was achieved. During maturation, type III collagen, which was prevalent during proliferation was replaced by type I collagen. Disorganized collagen fibers were rearranged, cross linked and aligned along tension lines improved skin texture and scar.

TCA 15% was a very light superficial chemical peeling. It produced very light stratum corneum exfoliation, wounding to stratum granulosum / papillary dermis depth. It considered as the main therapy in acne, could be added to other acne therapy such as retinoids and antibiotic. TCA had keratolytic effect by dissolved intercellular cement and reduced corneocyte adhesion and anti-inflammatory effect by commedolytic action in acne vulgaris. TCA was first line therapy for acne scar and skin rejuvenation. In high concentration was good for treating acne scar (CROSS/ Chemical reconstruction of Skin Scars technique).

Conclusion

As the other reviews and research, this research showed that acne was found most common in women at the age 15-23 years old. The mean of the age was 18,78 (95% CI 17,10 - 20,46) ± 2,81 years. Most samples were at the age of 16 years old (36%). The longer for the Length of the sickness of the samples was less than 1 year (64 %). The mean of length of the sickness was 1,71 years (95% CI 1.05 to 2,37) ± 1.09 years. Genetic was predisposition factor in 85,7% of samples, and acne triggered by cosmetic (42,9%), stress (28,6%), menstruation (92,3%) and diets (35,7%).

This research proved that one layer of 15% TCA superficial chemical peeling was statistically and clinically effective therapy to treat comedos, papule-pustules and all types of acne lession in acne vulgaris.The mean of difference of GAGS acne score before-after peeling was 13,07 (74,75%). The mean of difference of papulepustules before-after peelings was 5,14 (81,66%), comedos was 83,92 (85,23%) total acne lessions was 77,07 (86,79%).

The mean of Acne Score according to Global Acne Grading System before peeling was 16,78 (95%CI 10,61 to 22,95) ± 10,3. The mean of Acne score according to Global Acne Grading System after peeling was 3,71 (95% CI 1,72 to 5,7) ± 3,32. The mean of difference of acne score before-after peeling was 13,07 (95% CI 7,78 to 18,36) ± 8,82.The mean of difference percentage of acne score before-after peelings was 74,15% (95% CI 58,57% to 89,73%) ± 26,001%.

The mean of difference of papulepustules before-after peelings was 5,14 (95% CI 1,23 to 9,52) ± 6,52. The mean of percentage difference of papulepustules before-after peeling was 81,66% (95% CI 65% to 98,3%) ± 27,8%.

The mean of difference of comedos before-after peelings was 83,92 (95% CI 21,42 to 146,42) ± 94,18.

The mean of percentage difference of comedos before-after peeling was 85,23% (95% CI 74,09% to 96,36%) ± 16,78%.

The mean of difference of total acne lessions before-after peelings was 77,07 (95% CI 22,49 to 131,65) ± 91,09. The mean of percentage difference of total acne lessions before-after peeling was 86,79% (95% CI 76,95% to 96,62%) ±16,41%.

So, 15% of TCA had the best in comedolytic activity and also good to treat inflammation in papulopustules acne vulgaris. It could be applied as the single main therapy for all types of acne vulgaris or could be combined with other acne therapy (e.g. Retinoic acid) to solve resistance problems to antibiotic and antifungal.

TCA chemical peeling caused epidermal coagulation and collagen necrosis up to the upper reticular dermis, reepithelialization begun from survival islets of keratinocytes and skin appendages and the clinical effect were due to resultant increased in dermal volume of collagen, glycosaminoglycans and elastin. Keratolitic and comedolitic effect of TCA diminished hypercornification-ductal obstruction and bacterial-fungal colonization, so decreased inflammation. TCA superficial chemical peeling diminished free fatty acid that was important for bacterial and fungal growth, so it acted as antibiotic and antifungal adjunctive therapy. So, the goal of therapy of acne vulgaris: removed plugging of the pilar drainage, reduced sebum production, treated bacterial and fungal colonization, and prevented from scaring could be solved by 15% TCA superficial chemical peeling as one of acne treatment choices. It induced re-epithelialization and increased new collagen formation, resulted in skin tightening, glowing and rejuvenating, improving fine line and minimized acne scarring. Chemical peeling increased acidity of the acne skin patient and decreased Trans Epidermal Water Loss, so it improved skin barier of the acne patients better.

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