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ACNE VULGARIS, RECENT UPDATES ON PATHOPHYSIOLOGY, DIAGNOSIS AND TREATMENT- A SYSTEMIC REVIEW STUDY

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Abstract

Background: *Acne vulgaris is defined as inflammation in a chronic pattern of the pilosebaceous unit system consisting of hair follicle, hair shaft and sebaceous gland, acne is between the most common dermatological conditions worldwide, with an estimated 700 million people affected. Acne is labeled as a chronic disease due to its prolonged course, way of recurrence and relapse, and manifestations such as acute onset or slow onset. Moreover, acne causes a huge negative impact on psychological and social life. Acne vulgaris affects over 70% of teenagers, and persists beyond the age of 22 years in 4% of men and 15% of women. Lesions of acne may be manifested as inflammatory papules, comedones and pustules. In more severe cases it may develop into nodules and cysts. Moreover, it can cause scarring and psychological distress.*

Methods: *We conducted a systemic review study in which we used a wide range of databases, PubMed and Medline search engines searching for "Acne vulgaris pathophysiology, diagnosis and treatment", we excluded any unrelated topics and excluded acne vulgaris with comorbidities. We included all researches that deal with acne in all sexes and all age-group and all races.*

Results: *We found 32 systematic reviews and observational studies that met our inclusion criteria. We excluded 21 articles which were not according to our inclusion criteria.*

Conclusion: *In conclusion, this study shows that the recent updates on the diagnosis and new treatments related to acne vulgaris is effective and it is a good step toward the new treatment modalities in our dermatology specialty. However, we need more researches to be conducted in Europe, middle-east targeting such important and crucial topics.*

Key words: *acne, acne vulgaris, diagnosis, pathophysiology, treatment.*

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INTRODUCTION:

Acne vulgaris is defined as inflammation in a chronic pattern of the pilosebaceous unit system consisting of hair follicle, hair shaft and sebaceous gland, acne is between the most common dermatological conditions worldwide, with an estimated 700 million people affected. Acne is labeled as a chronic disease due to its prolonged course, way of recurrence and relapse, and manifestations such as acute onset or slow onset. Moreover, acne causes a huge negative impact on psychological and social life. Acne vulgaris affects over 70% of teenagers, and persists beyond the age of 22 years in 4% of men and 15% of women. Lesions of acne may be manifested as inflammatory papules, comedones and pustules. In more severe cases it may develop into nodules and cysts. Moreover, it can cause scarring and psychological distress.

However, there is an obvious improvement in understanding the pathophysiology of acne, the mechanisms of actions of available drugs to treat the disease, many unsolved questions remain. The lack of a clear grading system also slows efforts to compare efficacies of different medications in clinical studies, which is impeding the formulation of a globally approved consensus guideline. However, there are abnormalities in many processes (sebum production and sebocyte differentiation, proliferation and inflammation) can act to the development of acne, an extensive treatment regimen is needed in most patients.

This complicated pattern impairs compliance, which is the key for treatment success. Acne sometimes it may end up in scarring and post-inflammatory increased pigmentation, which has a negative impact on quality of life.

Novel delivery strategies for and modifications of existing drugs are recent changes in acne treatment, in addition to the development of new medications that target regulatory pathways involved in acne pathophysiology.

Moreover, there is myriad treatment options like, oral isotretinoin (an agent that blocks all the pathophysiological pathways of acne and has excellent adherence, and many advanced therapies in progress, improved treatment options will be available for patients soon. In this article we describe the following aspects of acne vulgaris: epidemiology, pathophysiology, diagnostic methods, available medications and new treatments.

Severity of acne; mild acne is defined as non-inflammatory lesions (comedones), a few inflammatory (papulopustular) lesions, or both. Moderate acne expressed as advanced inflammatory lesions, occasional nodules, or both, and mild scarring. Severe acne characterized as an inflammatory lesion, nodules, or both, and scarring.

Epidemiology

Most people experience acne during adolescence, with >85% of teenage boys and 75% of teenage girls affected. Almost 30% of these young people have moderate-to- severe acne, and as many as 40% continue to suffer from acne in adulthood. A systematic analysis for the Global Burden of Disease study indicated that acne was the eighth most prevalent disease globally in 2011.

Acne in Europe:

This large survey involving more than 10,000 individuals from seven European countries considered how acne is perceived, diagnosed and treated from the viewpoint of young people aged 15–24 years with self-reported acne.

Almost 40% of respondents had not had their acne diagnosed by a healthcare practitioner, indicating that a substantial proportion of people with acne do not seek medical help. This is consistent with the results from two other surveys, both conducted in France, in which 39% and 52% of people aged 12–25 years with self-reported acne said they had not gone to a physician. In contrast, a study in the USA found that 81% of adolescents aged 10–20 years had not seen a physician for their acne.

Among those respondents who reported that their acne was treated, the most common option was over-the-counter (OTC) topical products chosen with the help of a pharmacist (approximately 24%).

Acne in Belgium, Czech and Slovak Republics, France, Italy, Poland and Spain:

The overall adjusted prevalence of self-reported acne was 57.8% (95% confidence interval 56.9% to 58.7%). The rates per country ranged from 42.2% in Poland to 73.5% in the Czech and Slovak Republics. The prevalence of acne was highest at age 15-17 years and decreased with age. On multivariate analysis, a history of maternal or paternal acne was associated with an increased probability of having acne (odds ratio 3.077, 95% CI 2.743 to 3.451, and 2.700, 95% CI 2.391 to 3.049, respectively; both $P < 0.0001$), as was the consumption of chocolate (OR 1.276, 95% CI 1.094 to

1.488, for quartile 4 vs. quartile 1). Increasing age (OR 0.728, 95% CI 0.639 to 0.830 for age 21-24 years vs. 15-17 years) and smoking tobacco (OR 0.705, 95% CI 0.616 to 0.807) were associated with a reduced probability of acne.

Acne in the United States

Acne is the most commonly diagnosed skin condition in the United States according to the 2011 National Ambulatory Medical Care Survey (NAMCS) factsheet for dermatology[8], and accounts for more than 5 million visits to physicians each year[9]. However, acne was the most common disease seen by dermatologists in the United States and the thirteenth most common condition by non- dermatologists, resulting in the second most common reason for referrals to dermatologists[10].

Pathophysiology

Acne develops within the pilosebaceous unit and involves many processes. Important features underlying acne development include impaired sebaceous gland activity related to excessive sebum and alterations in sebum carboxylic acid composition, dysregulation of the hormone micro-environment, interaction with neuropeptides, follicular keratinization, induction of inflammation and dysfunction of the immunity system. These processes impair functioning of the pilosebaceous unit, which ends up in the transition of a standard pore to microcomedones, and further to comedones and inflammatory lesions. Bacterial antigens can potentiate the inflammatory process19–21. Genetic studies of heterozygous and homozygous twins and family studies have produced a growing body of evidence for the role of hereditary factors within the risk of acne develop- ment22–24. Acne may also be triggered or worsened by, as an example, ultraviolet illumination and other environmental factors25,26, dietary factors27,28, smoking29, stress and therefore the modern lifestyle30. (figure 3)

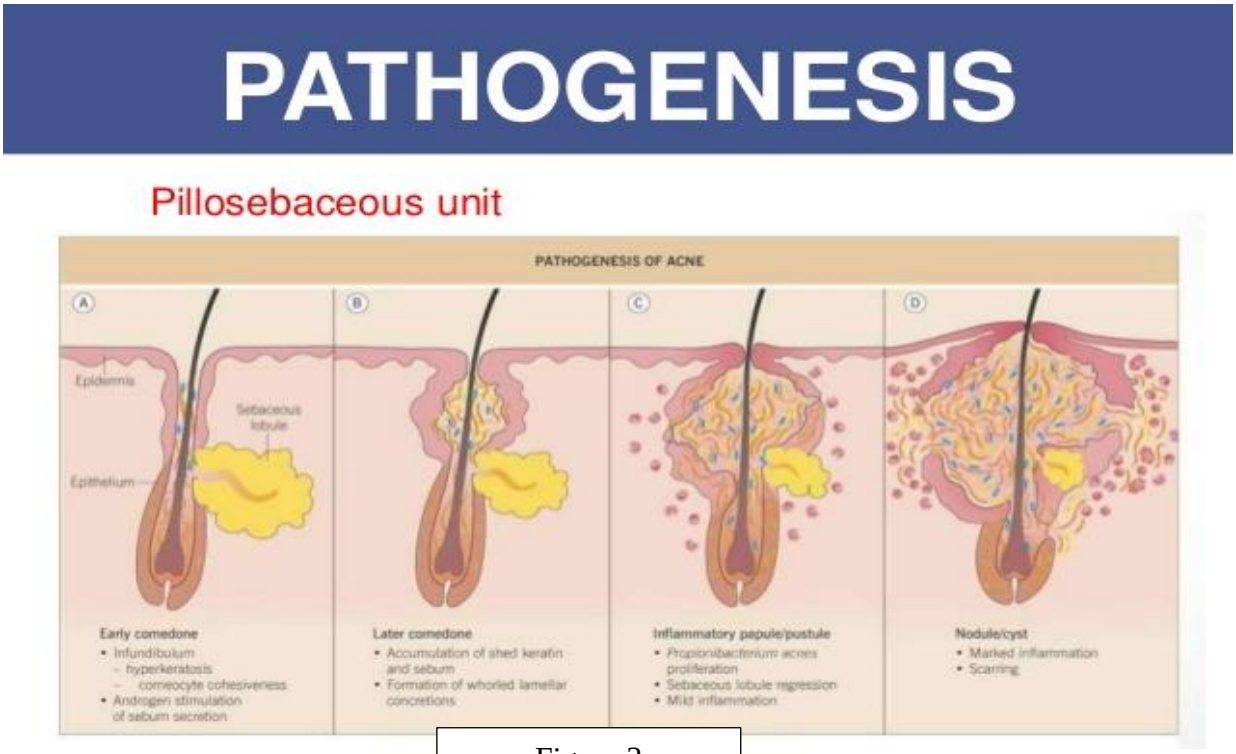

Figure 3

Sebum

Sebum is secreted by the glandulae sebaceae and comprises an oily mixture of triglycerides, wax esters, squalene, free fatty acids and tiny amounts of cholesterol, cholesterol esters and diglycerides. Sebum synthesis is managed by many factors that activate pathways involved in cell proliferation and differentiation, lipogenesis, hormone metabolism, and cytokine and chemokine release. Sebaceous lipid synthesis is more complicated than previously thought, as mediated hyperactivation of epidermal protein receptor— a serious group of proteins that coat lipid droplets — may additionally regulate sebocyte differentiation and lipid production.

Excessive sebum is assumed to be a key contributor to acne development. However, not all patients with acne experience hyperseborrhoea. However, the use between Sebum production is managed by many key factors that activate pathways involved in cell proliferation and differentiation, lipogenesis, hormone metabolism, and cytokine and chemokine release.

Acne is additionally associated with alterations within the free acid composition of sebum. Sebum of patients with acne contains less essential (that is, fatty acids that cannot be synthesized by the body and might only be acquired from the diet).

Systemic and native hormonal imbalance

Whether the primary abnormality causing acne is within the extent of circulating hormones or within the processing of hormones within the peripheral tissue is debated. However, usually acne starts in puberty when the hormone balance starts to alter dramatically.

In addition to systemic changes in hormone levels, local overproduction of steroids, specifically androgens, is said to acne. Sebocytes produce steroid hormones including androgens (testosterone and 5α-dihydrostestosterone (5α-DHT)), oestrogens (oestradiol and oestrone) and glucocorticoids (corticosterone and cortisol)47. Cutaneous steroid production could also be regulated by locally produced corticotropin-releasing hormone, corticotropin or cytokines47–49. Patients with acne produce more testosterone and 5α-DHT in their skin than healthy controls50, which reinforces sebaceous gland activity51,52 and stimulates sebocyte function, respectively40. Glucocorticoids also regulate the assembly of sebum.

Women and men with acne have high serum levels of insulin-like protein 1 (IGF1). However, In women, the IGF1 levels are used with the quantity of acne lesions, facial sebum excretion rate in post- adolescent patients and serum levels of 5α-DHT and DHEA sulfate.

Neuropeptides

The glandular sebaceous cell expresses functional receptors for several neuropeptides, including the receptor for corticotropin-releasing hormone, melanocortins, β-endorphin, vasoactive intestinal polypeptide, neuro- peptide Y and calcitonin gene-related peptide. Activation of these receptors in human sebocytes modulates the assembly of cytokines, cell proliferation and differentiation, lipogenesis and androgen metabolism. Substance P, can be induced by stress, may stimulate the proliferation of sebaceous precursor cells and increase sebaceous cell volume.

Inflammation cascades

Whether hyperkeratinization of the follicular duct pre-cedes the onset of inflammation or contrariwise is debated75. The outcomes of IL-1 existence was established to be high around nonincluded hair follicles before the observation of keratinocyte hyperproliferation and activation suggests an inflammatory trigger. However, once inflammation is started, inflammatory acne lesions upregulate many several genes, including those who encode matrix metalloproteinases, β-defensin 4, IL-8 and granulysin.

Nuclear factor-κB (NF-κB) is additionally activated in acne lesions79, as are the NF-κB-regulated cytokines like IL-1β, IL-8, IL-10 and tumor necrosis factor (TNF)80. However, TNF elicits lipid synthesis by JNK, PI3K and AKT pathways. high levels of IL-8 induce inflammatory cells, including polymorphonuclear leukocytes and lymphocytes. IL-17A-positive T cells and T helper 17 (TH17)-related cytokines are exited in acne lesions and might need a crucial role within the disease.

Moreover, metabolic pathways and several inflammatory lipid co-mediators are abnormal in acne lesions. Prostaglandins are synthesized by the cyclooxygenase (COX) enzymes. Sebocytes encode both COX isozymes, COX1 and COX2, and COX2 expression is selectively upregulated in sebaceous glands of patients with acne.

Propionibacterium acnes

The cutaneous microbiota may additionally be involved in acne pathogenesis. A metagenomic analysis showed that although the quantity of Propionibacterium acnes on the skin was similar between patients with acne (n = 49) and healthy

controls (n = 51), there were differences among populations in two groups. Certain P. acnes strains were highly associated with acne, whereas other strains were enriched on healthy skin88, which is important on condition that different P. acnes strains have different inflammatory potential. P. acnes type III is that the foremost pro- inflammatory strain and upregulates proteinase- activated receptor 2 (PAR2), TNF, matrix metalloproteinase 13 and tissue inhibitor.

Modern lifestyle, diet and smoking

The modern lifestyle, which has diet, stress, urban noise, socioeconomic pressure, light stimuli and variations in sleep patterns, could also be a possible risk factor for acne35,108. Diet might contribute substrates for synthesis of sebaceous lipids109, just like the essential acid polyunsaturated carboxylic acid. However, caloric restriction curtails sebum excretion, which is reversible by a customary diet111,112. However, changes in eating fat or carbohydrate can change and affect sebum production and composition. The apparent absence of acne in native non-Westernized people in Papua island and Paraguay also supports this notion114. Total cholesterol, lipoprotein (LDL) cholesterol, lipoprotein (HDL) cholesterol and apolipoprotein A1 were higher in patients with severe acne than in healthy, age-matched controls (n = 90); however, the degree in patients were within the traditional range.

Genetics

Genetics have a role within the development of acne, as evidenced by family and twin studies22–24,122. Several genetic polymorphisms affecting the expression and/or function of genes are investigated. Genes related to acne included the IGF1 (CA) 19 repeat poly- morphism123, the Pro12Ala polymorphism of PPARG124, the IL6-572 G/C polymorphism and therefore the IL1A-889 C/T polymorphism125; however, further studies during this field are needed.

Diagnosis, screening and prevention

Clinical presentation and grading

Acne affects body areas characterized by an increased density of pilosebaceous glands, like the face, chest and back130. The initial acne lesion is that the microcomedone, which is an invisible (to the naked eye) microscopic structure. During the course of acne, non-inflammatory lesions form, including closed (whiteheads) and open (blackheads) comedones, followed by inflammatory lesions that include superficial lesions like papules and pustules (≤5 mm in diameter) and deep pustules or nodules130.

Acne is diagnosed supported clinical examination and may be classified in line with severity, lesion type and age of onset. Acne may be classified as mild, moderate or severe and in an exceedinglyccordance with the lesions that predominate in a given patient: comedonal, papulo- pustular, nodular, nodulocystic or conglobate acne (acne conglobata)130. Acne conglobata could be a rare, the nose) is reliable137. Although stretching of the skin facilitates the visualization of comedones, it's not per- mitted for normal lesion counting because the degree of stretching might vary135. However, the good way of acne lesion contributing to staging of acne is that individual lesions are deeply measured and classified as either non-inflammatory or inflammatory lesions, which guarantees homogeneity and facilitates comparison of various results of studies on acne treatments. To locate deep lesions, palpation is additionally necessary because they're not detected with standard photographic methodology.

Acne staging systems are established to be used as a complementary, easy to use and rapid mode of acne grade testing and for the choice of eligible patients for treatment studies. Overall scales could be less quantitative but more relevant to clinicians and their patients. Currently, no overall acne grading system is taken into account to be a world standard, although efforts are underway to make a standard140,141.

Modern diagnostics through imaging

Many several images ways are there over the years to visualize acne and grade its severity, and to predict the response to treatments. Standard photo- graphs are a useful and reliable tool but must use the identical lighting, distance from the patient, camera and processing procedures. Furthermore, photographs are limited by the problem in distinguish deep lesions from active superficial lesions and are less accurate for non-inflammatory lesions134,135.

Moreover, modern photographic strategies have provided new chances for improving acne visualization and improving the accuracy of the assessment of acne severity and response to treatments. Hence, advanced imaging techniques include parallel polarization and orthogonal polarization imaging, stereoimage optical topometer imaging to construct three-dimensional stereoimages, and fluorescence photography. Parallel polarization

imaging enhances the visualization of skin surface features, like papules, pore size, skin oiliness and acne scars145. Orthogonal polarization photography enhances the visualization of inflammatory acne lesions, erythema and skin brightness. However, there is a Parallel- polarized and cross-polarized photography with video microscopy and sebum production measurement may be combined. Fluorescence photography using short wavelengths is wont to visualize P. acnes density supported the porphyrin production and therefore the corresponding orange– red fluorescence intensity.

Differentiation from other dermatological conditions

Acne is clinically heterogeneous and medical diagnosis is predicated on the sort of lesion, age at disease onset and persistence of acne in adulthood. The medical diagnosis is sometimes possible on clinical grounds and therefore the patient's medical history; however, when doubtful, laboratory tests, imaging or histopathological examination of a skin biopsy might have to be performed to exclude other conditions to ascertain an accurate diagnosis146. altogether cases, the presence of comedones could be a prerequisite for establishing diagnosis of acne147.

On the premise of the age of presentation, neonatal acne should be differentiated from skin infections (bacterial, viral or fungal), transient benign pustular eruptions (neonatal cephalic pustulosis, erythema toxicum neonatorum and transient neonatal pustular melanosis), milia, glandulae sebaceae hyperplasia, miliaria, infantile acne, acne induced by topical oils and ointments (acne venenata infantum), drug-induced acneiform eruptions and congenital adrenal hyperplasia19. The medical diagnosis of childhood acne includes perioral dermatitis and childhood rosacea146. More complex conditions which will have to be differentiated from acne include the synovitis acne pustulosis hyperostosis osteitis (SAPHO) syndrome, and pyogenic arthritis, pyoderma gangrenosum and acne (PAPA) syndrome19,148.

Prevention

The prevention of acne relies on the successful management of modifiable risk factors implicated in its development, including underlying systemic diseases and lifestyle factors. Acne could also be the cutaneous manifestation of an underlying systemic disease like congenital adrenal hyperplasia or polycystic ovary syndrome; in these cases, the timely and successful management.

Various lifestyle factors, like dietary habits, obesity and smoking, may influence the event of acne149. However, the effect of lifestyle interventions on acne remains a largely debated issue, as epidemiological studies have produced contradictory results, and well-designed trials that are ready to produce evidence-based results are largely lacking. Similarly, self-reported history of acne was positively related to intake of milk in a very prospective cohort study of 4,273 boys. Milk might influence comedogenesis through hormonal pathways, as milk contains androgens (precursors of dihydro- testosterone and other non-steroidal growth factors), or through higher levels of IGF1, which could affect the pilosebaceous unit150. A cross-sectional study in 1,871 patients with acne reported that frequent fat and sugar intake were related to increased risk of acne. However, other studies have didn't show an association between diet and acne. Considering these controversies, more studies are warranted.

Treatment

A large number of acne treatment products are available, and a large range of combination products are introduced, which provide numerous treatment options to varied patients with different preferences. However, large, well-designed, randomized controlled trials to assess and compare the effectiveness of acne treatment options are either lacking or have used different designs and methodologies, leading to a scarcity of strong evidence to support many of the recommendations in acne treatment guidelines. Hence, current guidelines depend on the opinions of experts. Furthermore, for acne related to systemic diseases, therapeutic information is usually at the extent of case reports.

Current guidelines for acne treatment include those from the world Alliance to enhance Outcomes in Acne6,157, the American Academy of Dermatology/ American Academy of Dermatology Association158, the eu Dermatology Forum Evidence-based (S3) guidelines for the treatment of acne159, the eu expert group on oral antibiotics in acne160, and therefore the Forum for the development of Clinical Trials in Acne position on isotretinoin161. Some general principles that form the inspiration of those guidelines are as follows. Acne is not any longer considered a natural a part of the life cycle, and to forestall its psychological and physical sequelae, early and aggressive treatment is critical. Longitudinal studies of the explanation of acne specializing in the role of early treatment in preventing persistent disease are yet to be conducted162.

As a multifactorial disease, combination therapy seems to be the foremost reasonable approach in most cases6. Guideline recommendations are categorized in line with acne severity and also the presence or absence of inflammation. Combination of a topical retinoid plus an antimicrobial agent is usually recommended as first-line therapy for many patients with acne, targeting multiple pathological factors in both inflammatory and non-inflammatory acne lesions. However, there are always exceptions for this general rule are severe acne and mild comedogenic or non-inflammatory acne. For mild comedo or non-inflammatory acne, treatment usually starts solely with a topical retinoid, whereas within the case of severe acne, oral isotretinoin therapy should be considered early. To limit antibiotic resistance, antibiotic monotherapy should be avoided. In mild-to-moderate acne, topical antibiotics should be used with bleaching agent (BPO) and a topical retinoid, and oral anti-biotics are better reserved for moderate-to-moderately severe acne; the duration of antibiotic use should be limited163. Isotretinoin remains the treatment of choice for severe acne, but several precautionary measures must be taken during an isotretinoin course.

Topical retinoids

Topical retinoids are axerophthol derivatives. The binding of retinoids to their receptors — the retinoic acid receptors and therefore the retinoid X receptors — in keratinocytes reduces follicular hyperkeratinization and reduces adhesion164. This effect not only leads to inhibition of comedogenesis but also might enhance the penetration of other topical acne medications.

However, retinoids have characteristic of anti-inflammatory effects by inhibiting the activation of the transcription factor AP1, and by downregulating the expression of TLR2. attributable to these comedolytic (that is, agents that split comedones and open up clogged pores) and anti- inflammatory effects, topical retinoids are recommended by the treatment option of the two comedogenic and inflammatory acne as an initial and maintenance treatment and to prevent relapses. Topical retinoids for the treatment of acne include tretinoin, adapalene, tazarotene (which isn't available in Europe), retinaldehyde and topical isotretinoin (the latter two aren't available within the United States), which are all available in various formulations and concentrations167. To pre- vent acne development or maintain improvement and avoid acne relapses, the applying of appropriate topical treatment is recommended159. the very fact that the microcomedone is that the initial microscopic acne lesion high- lights the requirement for applying topical acne therapies not only on clinically apparent lesions but also on the entire face to forestall the event of visible lesions159. However, because they must be applied to the full affected area, topical treatments often cause irritation and dryness. additionally, use of topical retinoids isn't recommended during pregnancy; Adapalene products tend to be the most tolerable of treatments. Topical retinoids are also reasonable choices for maintenance therapy after initial successful treatment.

Topical antimicrobials

BPO. BPO, an organic peroxide derived from a by-product of pitch, has become the foremost widely used topical acne medication in dermatology168. BPO treatment alone improves inflammatory acne157, and its mechanisms of action include antimicrobial, anti-inflammatory and keratolytic effects and wound-healing activity168. Although stronger than any prescription antibiotic against P. acnes, BPO remains safe for human use168. Low-strength (2.5% or 5%) BPO is suggested, because it is a smaller amount irritating than and as effective as higher concentration preparations169.

For BPO, like adapalene, the time to realize a 25% reduction within the mean number of inflammatory lesions doesn't change for various concentrations in patients with mild-to-moderate papulopustular acne. However, BPO gave the impression to act faster than topical adapalene, tretinoin and isotretinoin170. Some authors have suggested starting treatment with BPO alone for mild inflammatory acne, because of the price of retinoids, safety and good results162. BPO is additionally available as a fixed-dose combination product with adapalene that may help to cut back the complexity of treatment.

Topical antibiotics. Erythromycin and clindamycin are the foremost commonly used topical antibiotics in acne treatment, both of which are available in numerous formulations. Antibiotics (either topical or oral) don't seem to be intended to be a monotherapy for acne. as an example, topical antibiotics should only be utilized in combination with BPO to assist prevent the event of antibiotic- resistant bacteria. However, one limited fixed-dose gels of topical antibiotics with BPO are effective, more as a combined gel formulation of clindamycin with tretinoin. Hence, clindamycin and BPO combination seem to work quicker than adapalene; this mixture may well be faster than BPO alone, but more studies are needed to

verify this result170. a mix of adapalene and BPO which of clindamycin and BPO have comparable times to attain a 25% reduction in lesion count170,171. Dapsone gel could be a newer topical antibiotic choice. Although the mechanism of action of Dapson isn't yet clear, it's shown good ends up in studies and various new options are in development174.

Other topical agents

Salicylic acid may be a topical medication present in many over-the-counter products, which has comedolytic effects but is also less effective than retinoids. Another topical agent, azelaic acid, has antibacterial, comedolytic and anti-inflammatory properties and is taken into account as a possible first-line monotherapy for female adult patients with acne, and an honest choice for maintenance therapy due to its good tolerability and safety175. a possible adverse effect of azelaic acid is hypopigmentation, which could be helpful in treating post-inflammatory hyperpigmentation. Although most publications have investigated the 20% azelaic acid cream formulation, the 15% gel was as efficient as BPO and topical clindamycin for patients with mild-to- moderate acne176. a unique study using the cyanoacrylate technique — an explicit method for microcomedone assessment — in patients with mild-to-moderate acne has shown the same effect for azelaic acid 15% gel compared with 0.1% adapalene 177.

Oral antibiotics

There are several medications, like doxycycline and minocycline are effective and have replaced tetracycline and erythromycin in most cases of acne therapy. However, Tetracycline, minocycline and doxycycline are contraindicated in pregnancy and in children <10 years of age; erythromycin is only recommended in these cases. Azithromycin isn't commonly used thanks to the chance of skyrocketing resistance, which may be a crucial issue in other dis-eases. As tetracyclines control acne through their direct anti-inflammatory effects additionally to their antibiotic property, using subantimicrobial doses of doxycycline is promising, but more investigation is required during this field. Although minocycline is effective in acne treatment, its superiority to other tetracyclines has not been proven178. Extended-release minocycline has shown good ends up in acne treatment179, and co-trimoxazole is another for severe acne. Several studies have compared the efficacy of various antibiotics in acne therapy, but no antibiotic demonstrated superior results.

To reduce the event of antibiotic resistance, systemic antibiotic therapy must always be combined with a topical retinoid or BPO and may be limited to a period of three months180; 4–6 weeks after the beginning of treatment is that the appropriate time for response assessment160.

Concomitant treatment of oral and topical antibiotics, and use of topical antibiotics without BPO should be avoided6. However, an analysis of published data of 29,908 patients from 2008 to 2010 demonstrated that the mean duration of oral antibiotic therapy was 129 days — for much longer than indicated. Simultaneous topical retinoid therapy didn't occur in 57.8% of treatment courses181. There has been a shift towards non-antibiotic treatment in acne management182, but there's still the requirement to tell all physicians about the importance of short (<3 months) regimens in numerous settings. A study of patients with preadolescent acne found that dermatologists predominantly prescribe topical retinoids for this people, whereas medical aid physicians prescribe antibiotics, particularly oral anti- biotics183. That is, medical aid doctors aren't aware of using adapalene in teenagers.

Hormonal therapy

Hormonal agents that reduce androgen activity may be given to scale back sebum production in women. Oral contraceptives and, in some countries, spironolactone are commonly prescribed hormonal therapies. the employment of anti-androgen treatment isn't limited to acne induced by hyperandrogenism; this therapy also improves acne in women with normal serum androgen levels157. Hormonal therapy is prescribed together with other acne medications for postmenarcheal to premenopausal women with moderate-to-severe acne who don't will become pregnant. additionally, they're going to improve even mild acne in patients who use this medication for contraception, cycle irregularities or patients who experience cyclical acne flares184. Hormonal therapy could also be underused in women with acne185.

It takes 6–12 months before one can evaluate hormonal therapy results186. Meta-analyses of previous publications demonstrated that, although antibiotics may well be superior at 3 months, oral hormonal anti-androgens are such as antibiotics at 6 months in reducing acne lesions and, therefore, may be a more robust first-line alternative to systemic antibiotics for long-term acne management in women186,187. There are multiple oral hormonal

anti-androgens on the market; patient preference, cost and adverse-effect profile should determine the acceptable choice185.

It takes 6–12 months before one can evaluate hormonal therapy results[186]. Meta-analyses of previous publications demonstrated that, although antibiotics might be superior at 3 months, oral hormonal anti-androgens are equivalent to antibiotics at 6 months in reducing acne lesions and, therefore, could be a better first-line alternative to systemic antibiotics for long-term acne management in women[186,187]. There are multiple oral hormonal anti-androgens on the market; patient preference, cost and adverse-effect profile should determine the appropriate choice[185].

relationships, education about the pathophysiology of acne and considering the patient's preference for the topical delivery vehicle can improve adherence. More frequent visits to the physician increases adherence, and is superior to a regular visiting schedule and daily reminder phone calls to patients and parents205,206.

Evaluation of the psychiatric morbidity, especially anxiety and depression, is also beneficial. Most topical acne treatment products cause irritation; informing patients of possible adverse effects, providing written instruction on a way to manage irritation and dryness and considering alternative treatments are helpful strategies during this case207. A helpful consider adherence improvement is that the use of fixed-dose combination products208,209. Several antibiotics and BPO combinations are available, and an adapalene and BPO combination adheres to both the BPO and therefore the retinoid guidelines6. Although fixed-dose combination topical formulations may be a part of a safer and less expensive alter- native model to oral isotretinoin for treating severe acne, the high adherence of isotretinoin treatment is very important to stay in mind. in a very retrospective cohort study of 24,438 patients from 2004 to 2007 using the Marketscan Medicaid Database. Patients were most adherent to oral retinoids than the other acne drug classes (MPR: 0.78; 57% adherent) and therefore the least adherent to oral antibiotics (MPR: 0.21) and topical retinoids (MPR: 0.31)210.

Acne scars

Scars are important permanent sequelae of acne Up to 95% of patients with acne have scars, with 30% developing severe scars213. However, there is no of the currently available treatments achieve complete resolution of scars. Prevention of scars by early and aggressive acne treatment remains the simplest option. There are numerous medical, surgical and procedural options that may help to realize profound cosmetic improvement in acne scars. Using these methods together can even be more successful6,214. There are two main varieties of acne scars looking on the tissue response to inflammation: scars caused by increased tissue formation (hypertrophic and keloidal scars) and scars caused by loss of tissue (atrophic scars). Atrophic acne scars are more com- mon than keloids and hypertrophic scars, and may be divided into three subtypes: icepick or V-shaped, rolling or M-shaped and boxcar or U-shaped. Keloidal scars are more common in darker-skinned individuals215. (Figure 1 & 2).

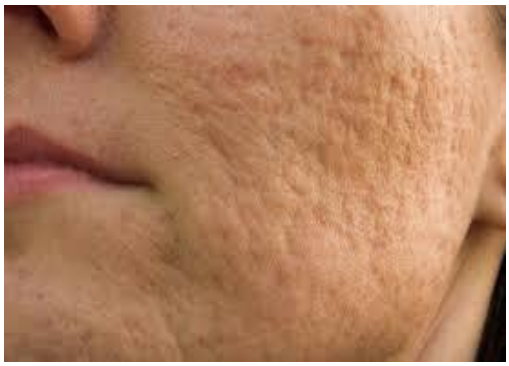

Figure 1

Figure 2

Quality of life

The WHO defines quality of life because the individual's perception of the position in life within the context of the culture and value systems within which someone lives and in relevancy his or her goals, expectations, standards and concerns. Acne lesions modify the individual's perception and affect every aspect of private, social, vocational and academic life 217. Patients with severe acne have higher unemployment rates than those without acne. However, Acne includes a severe impact on a patient's emotions, annoyance due to physical symptoms pain and itch and daily discomfort as a result of treatment. Patients with acne usually experience social anxiety and shame; they avoid eye contact, grow their hair long to hide the face, use makeup and choose a particular clothing style to attenuate the looks of acne lesions219,221,222. Acne is related to an increased risk of depression, anxiety and body dissatisfaction211. Depression is 2–3-times more prevalent in patients with acne than within the general population, and therefore the rate of depression was twice as high in women with acne than in men224,225. Patients with mild-to-moderate acne even exhibit

higher depression scores than patients with alopecia, atopic eczema or psoriasis. Although acne may be more psychologically damaging to adolescents than adults, the next prevalence of depression in older patients with acne has been observed226. Suicidal ideation rates were higher among patients with acne than patients with general medical conditions226.

Acne alone is also a source of stress and anxiety, but stress can even trigger or exacerbate acne even after con- trolling for changes in diet and sleep habits; a positive feedback can occur. Neuroimmunological research may pro- vide the primary insight into the links between acne stress and quality of life228,229.

The most frequent lesions related to greater impairment are cysts and nodules; even those that have only comedones report symptoms (itch and pain) and emotional effects (decreased self-esteem, difficulties in building relationships and social activities). However, the effect of acne on quality of life doesn't always correlate with acne severity. For this reason, recognition of clinical and pertinent psychological signs must be taken into consideration when individualizing treatment.

CONCLUSION:

In conclusion, this study shows that the recent updates on the diagnosis and new treatments related to acne vulgaris is effective and it is a good step toward the new treatment modalities in our dermatology specialty. However, we need more researches to be conducted in Europe, middle-east targeting such important and crucial topics.

Contributors

All authors had full access to all of the data (including the statistical report and tables) and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Ethical approval

Ethical approval was not needed for this systemic review study.

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