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Acne vulgaris in adolescents – the review

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Abstract
Acne vulgaris is one of the most common chronic inflammatory skin disorders that affects almost 90% of the adolescents worldwide. Due to its effect on one's appearance, it causes not only physical but also psychological consequences. The cause of acne involves increased sebum production, hyperkeratinisation of the follicle, bacterial colonization and inflammation, which result in formation of comedones, papules, pustules and nodules. Diet, Body Mass Index, hyperhidrosis and stress can be triggering factors. The pharmacological treatment of acne involves substances administered topically as well as orally. First line of treatment of mild-to-moderate acne involves topical benzoyl peroxide, retinoids, chemical peels, antibiotics and combinations of those agents. The treatment of moderate-to-severe or inflammatory acne consists of oral antibiotics, isotretinoin, oral contraceptives and spironolactone. New therapies are being investigated and show a great potential, however further research should be pursued in order to achieve long-lasting results of the treatment.

Keywords: adolescent acne, acne vulgaris, skin disorder

Introduction
Acne vulgaris (hereafter acne) is one of the most common chronic inflammatory skin disorders, affecting almost 90% of the adolescents worldwide[1]. It is caused by increased sebum production, follicle hyperkeratinisation, bacterial colonization and inflammation. Clinical presentation involves open or closed comedones, papules, pustules and nodules that are mostly localized on the face and neck, but can also develop on the chest, back and buttocks[2]. Although there is no mortality associated with acne, the condition due to its visible nature may negatively influence psychological wellbeing[3]. That is why it is essential to understand the nature of the disease and find a suitable and effective treatment for everyone.

Epidemiology
Acne vulgaris is commonly observed in adolescents and young adults. Adolescent acne begins at puberty, when the levels of sex hormones start to increase. The occurrence of acne among girls increases from 61% at age 12 years up to 83% at age 16 years, whereas in boys it increases from 40% up to 95%, respectively[2]. In contrast to adulthood where there is a female predominance, during adolescence this disorder is more common in males, especially with more severe forms of acne[4]. Western Europe, North America and Latin America are reported to have the highest prevalence of acne. Moreover, this disorder is considered to be the 8th most common disease in the world, as it affects people from adolescence up to the early thirties[5].

According to Zaenglein et al. acne affects approximately 50 million people in the United States (US). Despite appearing in most age groups, acne occurs in 85% of teenagers in the US[3]. Although there is no mortality connected to this disorder, it is associated with significant physical and psychological morbidity. The remaining permanent scars and pigmentation combined with negative effect on psychological wellbeing, may lead to poor self-esteem, anxiety and finally depression[6].

Pathophysiology and clinical presentation

Although the current understanding of acne pathogenesis is constantly evolving, it involves few key pathogenic factors such as excess sebum production, hyperkeratinisation in the pilosebaceous follicle, colonisation by *Cutibacterium acnes* (*C. acnes*) and inflammation caused by complex immune reactions[6]. What is more, it is suggested that high levels of androgens, diet and genetic factors may all be involved in the acne development[3].

The clinical presentation of acne starts with a primary lesion, which is called a microcomedo and is caused by the follicular hyperkeratosis that obstructs the flow of sebum onto the surface of the skin[2]. It is a precursor for all clinical manifestations of acne. Microcomedos evolve into other acne lesions such as comedones knows as whiteheads, open comedones known as blackheads and inflammatory pustules, papules and nodules[7].

The microcomedo is a suitable environment for *C. acnes* proliferation, population of which increases significantly during puberty, which causes higher secretion of pro-inflammatory mediators that cause an inflammatory response[8]. Cytotoxic free fatty acids are released into the skin due to follicular breakdown and contribute to the inflammatory reaction. Furthermore, the production of pro-inflammatory cytokines (IL-1, IL-8, IL-12) and defensins is initiated by recruited inflammatory cells and leads to the formation of inflammatory papules, pustules, and nodules[2].

The role of genetics in acne development is substantial, as the risk of developing acne in individuals with affected first-degree family member is estimated to be as high as 3 times greater than in individuals without a family history of acne[7].

Acne vulgaris occurs most commonly in areas of the body with abundant number of sebaceous glands, such as face (in 92% of cases), back (61%) and chest (45%)[6]. Neck and proximal upper extremities can also be affected by inflammatory and non-inflammatory lesions[2].

There are several clinical variants of acne. Acne conglobata, which is a severe and highly inflammatory type of acne occurs mostly in young males. It is characterized by the presence of grouped comedones, painful lesions and interconnecting deep-seated foul-smelling abscesses, located mainly on the face, chest, back, thighs and the buttocks. It may lead to significant scarring and disfigurement[9]. Another variant of acne is acne fulminans, a rare form that is characterized by sudden appearance of ulcerative nodules and haemorrhaging pustules paired with high fever, weight loss, bone lesions and elevated liver enzymes[10,11]. Neonatal acne, infantile acne, mid-childhood and preadolescent acne are prepubertal conditions and they do not occur as often as adolescent acne[2,12].

Triggering factors

The evidence connecting diet and acne is increasing. Scientists discovered a significant relationship between acne severity and dietary factors. High consumption of milk, cheese, yoghurt, chocolate and low consumption of vegetables, fruits and fish is closely associated with adolescent acne morbidity[13,14]. Although there are contradictory results regarding the relationship between Body Mass Index (BMI) and acne, most studies showed that individuals with higher BMI have elevated risk of the disease[15]. Additionally, the obesity in female adolescents with Polycystic Ovary Syndrome leads to insulin resistance and hyperinsulinemia, which results in hyperandrogenism and high levels of free testosterone, finally resulting in acne[4,14,16].

Another factor taken into consideration while assessing factors that trigger acne is hyperhidrosis. Although there are not many studies that confirm a clear relationship between excessive sweating and acne, a review conducted by Kutlu et al. reports that acne is indeed aggravated by sweating and exposure to hot weather[4].

Furthermore, individuals that are exposed to emotional stress may also be more prone to acne. Stress stimulates androgen hormones production. It also may alter the adrenal-pituitary axis, resulting in higher levels of cortisol. Moreover, the risk of inflammation and scarring is higher by stress-induces skin-picking and excoriations[4].

Treatment

When it comes to treatment of acne, a holistic approach is essential. The goals of therapy are to minimize scarring, provide the patient with the best appearance possible and manage psychological consequences. The first line of treatment for mild-to-moderate acne are topical agents, which have a favourable safety profile. For moderate-to-severe acne and acne that does not respond to topical agents, systemic therapies are usually prescribed[2].

The most common topical acne therapies include benzoyl peroxide, antibiotics, retinoids, combination of antibiotics with benzoyl peroxide, retinoid with benzoyl peroxide, retinoid with antibiotic, salicylic and glycolic acid[3].

Benzoyl peroxide is an antibacterial agent active against *C. acnes*. It also has anti-inflammatory properties, as well as comedolytic activity. The treatment of acne can be carried out with benzoyl peroxide alone or in combination with salicylic acid, retinoid, zinc or antibiotics such as clindamycin or erythromycin[17].

The retinoids are vitamin A derivatives, which inhibit the formation of new lesions, (such as comedones as well as inflammatory and non-inflammatory lesions) by decreasing cellular proliferation and differentiation[18]. Retinoids also have anti-inflammatory properties[19]. What is more, they reduce and prevent the appearance of dyspigmentation and atrophic scars[20]. There are three retinoids viable for topical treatment: tretinoin, adapalene and tazarotene. Although those agents can enhance any topical acne regimen, their use may be limited by the side effects such as dryness, peeling and irritation, which often results in the discontinuation of the treatment[21]. Furthermore, topical retinoid agents have been associated with an increased risk of photosensitivity, which is why daily sunscreen application is required. Although the therapy with retinoids in children <12 years of age is limited, a few changes have been recently introduced.

The combination of 2.5% benzoyl peroxide with 1% adapalene gel has been approved in patients ≥9 years old as well as 0.05% micronized tretinoin gel for patients ≥10 years of age[3].
Chemical peeling is a process used in treatment of acne that causes controlled chemical injury to the skin and removal of superficial lesions resulting in regeneration of new tissues[22]. Glycolic acid (GA) is a water-soluble alpha-hydroxy acid and is used in treatment as a chemical peel. High concentrations of GA (20-70%) have proved to be effective in acne treatment, however such concentrations should only be used in the hospital or dermatology clinic[23]. GA in low concentrations (<10%) may be beneficial to the skin and can be safely used at home[24]. Another chemical peel used is acne treatment is salicylic acid (SA), a Beta-hydroxyl acid with keratolytic and anti-inflammatory properties. Although SA is not toxic when applied with caution and can be used for all stages of active acne, it can be toxic when applied to large area. Such toxicity is called Salicylism and is usually associated with systemic absorption and high concentration of the acid. Both GA (30-70%) and SA (30%) are considered to be effective in treatment of acne[25].
Overall, when it comes to topical treatment of acne, topical treatment combinations are significantly more effective that topical agents used as a monotherapy[26].
The first line of systemic treatment for moderate-to-severe or inflammatory acne are oral antibiotics. As monotherapy of oral antibiotics in acne treatment is not recommended, they should be combined with topical retinoids and/or benzoyl peroxide. Although the most common antibiotics prescribed for acne treatment are tetracyclines, which penetrate the pilosebaceous unit, macrolides are also prescribed to patients that cannot use tetracyclines[27]. What is more, in order to avoid development of antibiotic resistance, oral antibiotics should constitute a bridge to other oral therapies and should not be used longer that 6 months[20,28].
Severe recalcitrant cases of acne vulgaris may be treated with isotretinoin, a retinoid that reduces the size of sebaceous glands, regulates cell proliferation, lowers sebum excretion and decreases keratinization. It also possesses anti-inflammatory and immunomodulatory properties that can be used for various skin diseases, not only acne[29]. Moreover, oral isotretinoin could be an effective treatment option for reducing the size of scars and their severity and at the same time improving the elasticity of the skin[30]. Although it is highly effective, isotretinoin has some adverse effects. Many patients may suffer from xerostomia (dry mouth), xerosis (dry skin), dry nose, ophthalmic changes, laboratory abnormalities as well as sun sensitivity and 90% of individuals will likely develop dry lips and cheilitis[31]. Isotretinoin is also highly teratogenic, which is why women of childbearing age should not be given oral isotretinoin until pregnancy is excluded and an effective contraceptive agent is administered[32].
For women in post-menarche with moderate-to-severe acne typically over the age of 15 years the use of oral contraceptives should be considered. Oestrogens present the ability to suppress the stimulatory effects of androgens allowing to decrease the size and activity of sebaceous glands. However, oral contraceptives have some adverse effects such as headaches, moodiness, nausea, bloating, breast tenderness, hypertension and, most severe, thromboembolisms[2,33].
Spironolactone is a potassium-sparing diuretic that has an anti-androgenic effect[34]. It is used in women that have elevated levels of androgens and are refractory to topical acne agents[2].

Since spironolactone showed similar efficacy compared to oral antibiotics, it is recommended as first choice while establishing the course of the therapy, as the risk of antibiotic resistance is growing[35,36]. Breast enlargement and tenderness, menstrual irregularities, headache, nausea, diarrhoea, vomiting, orthostatic hypotension and hyperkalaemia are possible side effects[2].
Other than the aforementioned, new forms of acne treatment are being developed. Anti-acne microneedle patches have been investigated by Tai et al. and showed to be a safe and effective treatment in acne and post-inflammatory hyperpigmentation, without adverse skin reactions[37]. What is more, inflammatory and non-inflammatory acne in adolescent can be safely controlled with the intralesional platelet-rich plasma injections and 1064 nm long-pulsed Nd:YAG laser[38].

Conclusions

Despite significant advances in the treatment of acne vulgaris, it remains a great inconvenience for not only adolescents, but also other age groups. Although most acne therapies are effective, the results are often not long-lasting, which may be frustrating for patients that struggle with long-term treatment. New approaches in therapy are promising, however, there should be more research dedicated to the area of the post-treatment results.
In conclusion, acne vulgaris is a condition that affects not only physical, but also psychological aspects of patients' life, thus the approach to treating the disease should be holistic.

Disclosure

Author's Contribution

Conceptualization - Aleksandra Wójcik; Methodology - Aleksandra Wójcik, Sylwiusz Niedobylski, Joanna Wrona, Daria Madycka, Kinga Wnuczek, Jakub Starownik, Kacper Michta; Software - Aleksandra Wójcik, Sylwiusz Niedobylski, Joanna Wrona, Daria Madycka, Kinga Wnuczek, Jakub Starownik, Kacper Michta; Check - Aleksandra Wójcik, Sylwiusz Niedobylski, Joanna Wrona, Daria Madycka, Kinga Wnuczek, Jakub Starownik, Kacper Michta; Formal analysis - Aleksandra Wójcik, Sylwiusz Niedobylski, Joanna Wrona, Daria Madycka, Kinga Wnuczek, Jakub Starownik, Kacper Michta; Investigation - Aleksandra Wójcik, Sylwiusz Niedobylski, Joanna Wrona, Daria Madycka, Kinga Wnuczek, Jakub Starownik, Kacper Michta; Resources - Aleksandra Wójcik, Sylwiusz Niedobylski, Joanna Wrona, Daria Madycka, Kinga Wnuczek, Jakub Starownik, Kacper Michta; Data curation - Aleksandra Wójcik, Sylwiusz Niedobylski, Joanna Wrona, Daria Madycka, Kinga Wnuczek, Jakub Starownik, Kacper Michta; Writing (rough preparation) - Aleksandra Wójcik, Sylwiusz Niedobylski, Joanna Wrona, Daria Madycka, Kinga Wnuczek, Jakub Starownik, Kacper Michta; Writing (review and editing) - Aleksandra Wójcik, Sylwiusz Niedobylski, Joanna Wrona, Daria Madycka, Kinga Wnuczek, Jakub Starownik, Kacper Michta; Visualization - Aleksandra Wójcik, Sylwiusz Niedobylski, Joanna Wrona, Daria Madycka, Kinga Wnuczek, Jakub Starownik, Kacper Michta; Supervision - Aleksandra Wójcik; Project administration Aleksandra Wójcik;

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