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Acne vulgaris during pregnancy – management ensuring both maternal and fetal safety

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ABSTRACT

Introduction and aim. Acne vulgaris represents a condition commonly encountered by women during pregnancy. However, its treatment becomes particularly demanding when occurring during gestation. The aim of this review is to present multiple strategies for management of acne in pregnant women, prioritizing both maternal and fetal safety.

Material and methods. Review and analysis of the scientific literature available in November and December 2023.

Analysis of literature. The study describes commonly used topical treatments and oral medications emphasizing difficulty and responsibility of assessing the safety of drug use during pregnancy. Apart from that, the importance of skin care is stressed with a focus on usage appropriate to the condition and pregnancy-safe cosmetics. The influence of diet and physical activity on acne development is also underlined, as well as the significant association between acne and mental health.

Conclusion. Dealing with acne during pregnancy might be difficult; however, there are effective and safe acne treatments suitable for pregnant women, along with various supportive approaches. Considering above, the authors highlight a holistic nature of acne management that includes not just medication but also procedural interventions, skin care practices, diet, physical activity, and psychological support.
Keywords. acne vulgaris, dermatology, pregnancy

Introduction

Acne vulgaris is a chronic inflammatory skin condition frequently encountered by women during pregnancy. It is estimated that up to 42% of gravidas suffer from acne and the vast majority of them had the condition pre-existing before pregnancy.[1,2] The clinical manifestation of the disease includes different types of skin lesions. These can be classified into primary non-inflammatory lesions (microcomedones, closed comedones, open comedones), secondary inflammatory lesions (papules, pustules, nodules, cysts, abscesses), as well as post-inflammatory lesions and scars. The severity of acne may differ, starting as isolated scattered comedones and very few papules and pustules up to more intense inflammatory changes with the presence of nodules or cysts.[3]

During pregnancy, acne tends to be inflammatory and spreads to the trunk region,[4] however its severe form is typically rare during this period.[5] Interestingly, throughout gestation, the intensity of acne can either escalate, alleviate, or remain unchanged, but the exact mechanisms by which pregnancy modifies its course in individual cases remain unclear.[6] Nevertheless, it is noted that due to heightened maternal androgen levels affecting sebum production acne tends to aggravate in the third trimester.[7] Besides hormonal changes, immunologic and metabolic factors associated with pregnancy may also contribute to the development of acne during this period.[7-9]

Even though sometimes trivialized as a purely cosmetic issue, acne exerts a substantial impact on the well-being and social interactions of individuals.[6] Moreover, combination of physiologic changes in female's bodies and rather difficult to predict character of the acne during pregnancy may be especially aggravating.[9] Unfortunately, while there is a broad range of pharmacological possibilities for treating acne vulgaris, the options become more limited when dealing with this condition during pregnancy, primarily due to the potential risks to the developing fetus.[6] Therefore treatment of acne in this situation can be challenging and the absence of sufficient clinical studies on the safety and effectiveness of common acne medications during gestation also complicates the decision-making process.[4]

Aim

Management of acne vulgaris should focus on mitigating and resolving skin lesions, preventing their consequences like scarring and discoloration, and concurrently enhancing the patient's quality of life.[3] In this review, we discuss various approaches to the management of acne in pregnant women, ensuring both

maternal and fetal safety. However, our publication emphasizes that the therapeutic approach should extend beyond pharmacological interventions, incorporating dermatological procedures, appropriate daily skincare routines, dietary considerations, physical activity, and essential psychological support. In other words – we underscore the holistic nature of acne management during pregnancy, recognizing the importance of a comprehensive approach that surpasses conventional pharmaceutical treatments.

Material and methods

Review and analysis of the scientific literature available in November and December 2023. The articles were searched on Google Scholar and PubMed using combined keywords (in both Polish and English languages): acne, acne vulgaris, pregnancy, treatment, management, safety, dermatology, procedural interventions, skin care, cosmetics, diet, physical activity, psychological support. Google search engine was also utilized, along with Polish-language scientific textbooks related to the topic of the study. No specific inclusion and exclusion criteria were defined. The writing of this manuscript involved the use of ChatGPT as a tool for assistance in translation, paraphrasing and linguistic proofreading the text.

Analysis of the literature

Topical treatments

Topical agents often mentioned in the context of treating acne vulgaris in pregnant women include:[4,9,10]

- benzoyl peroxide,
- azelaic acid,
- salicylic acid,
- antibiotics.

Benzoyl peroxide demonstrates antibacterial effects against *Cutibacterium acnes*, a bacterium strongly linked to acne, as well as sebostatic and keratolytic properties. Its optimal effectiveness is observed when used in combination with other acne therapies.[11] Benzoyl peroxide is typically applied once a day in various forms, such as gel or cream, with concentration available from 2.5% up to 10%.[12] However, research suggests that its higher concentrations are not significantly more effective than 2.5%.[12,13] Furthermore, 2.5% is generally better tolerated and may reduce the likelihood of skin irritation.[12] Approximately 5% of benzoic acid undergoes systemic absorption, but it is rapidly excreted unchanged in the urine.[14,15] Consequently, the associated risk of causing congenital malformations is very low, making it considered safe for use on limited skin areas by pregnant women (despite being previously perceived as potentially dangerous).[16,17]

Topical application of 20% cream or 15% gel forms of azelaic acid is another well-established therapeutic approach for acne vulgaris.[18] Azelaic acid exhibits antibacterial, anti-inflammatory, and keratolytic properties, hence the precise mechanism by which this substance treats acne is likely complex.[19]Similarly

to benzoyl peroxide, approximately only 4% of azelaic acid applied to the skin is being systemically absorbed.[9,20] In the context of our publication's topic, there are limited studies on the use of azelaic acid in pregnant individuals; however, the available ones have not reported any adverse effects on fetal development. Consequently, azelaic acid is generally regarded as safe for topical use throughout all trimesters of pregnancy.[4] Nevertheless, some authors recommend applying this substance only on small skin areas and advise against its use in the first trimester.[14,21]

Another popular acid – salicylic acid – is not as effective against acne as the substances mentioned before.[22] In any case, its reasonable usage (over small skin areas, not for prolonged time or under occlusive dressings) is generally considered safe throughout all stages of pregnancy, as its minimal systemic absorption is acknowledged.[4]

Topical acne treatment for pregnant patients can also encompass the use of antibiotics, especially erythromycin and clindamycin, which are characterized by anti-inflammatory, strong antibacterial, and mild comedolytic properties. Primarily applied in the form of solutions, topical antibiotics rarely cause irritations and are well-tolerated.[23,24] When applied topically to the skin, erythromycin and clindamycin result in minimal systemic absorption, making them safe for use during all trimesters of pregnancy.[4] Unfortunately, the use of local antibiotics in acne treatment can lead to the development of bacterial drug resistance, which is a notable drawback of this approach.[24] To mitigate that risk, it is advisable to combine all topical antibiotics with an additional antimicrobial agent, such as benzoyl peroxide.[24,25]

Topical retinoids also have a central role in acne vulgaris therapy, but the use of retinoic acid and its derivatives is generally contraindicated for pregnant women due to the potential risks to the developing fetus. Retinoids, such as isotretinoin, have been associated with congenital malformations, making it advisable to avoid their use during pregnancy. This applies to both topical and oral treatments.[12,14] Nevertheless, it is worth noting that in regards to the safety of using topical retinoids in pregnant women, there have been contradictory reports. While some studies suggest limited use may be safe, most experts advise caution and avoiding topical retinoids during pregnancy due to potential risks.[4] Table 1 provides information regarding the properties of acne topical treatments and their safety during pregnancy.

Table 1. Acne treatment during pregnancy – topical treatments[4,11,14,16,19,21-24]

Topical treatment	Properties	Safety during pregnancy
Benzoyl peroxide	• antibacterial • sebostatic • keratolytic	Safe for use by pregnant women on limited skin areas

Azelaic acid	• antibacterial • anti-inflammatory • keratolytic	Generally considered safe for use throughout all trimesters of pregnancy Some authors advise against its use in the first trimester
Salicylic acid	• keratolytic	Generally considered safe for use throughout all trimesters of pregnancy
Antibiotics (erythromycin and clindamycin)	• antibacterial • anti-inflammatory • comedolytic	Safe for use during all trimesters of pregnancy
Retinoids (isotretinoin)	• keratolytic • anti-inflammatory	Not recommended during pregnancy

Oral medications

Oral isotretinoin is regarded as the foremost efficacious anti-acne medication, recommended for severe acne and, in less severe cases, when other methods prove ineffective. Additionally, it is prescribed in situations of significant psychological distress triggered by the condition.[26] Nevertheless, as mentioned earlier, it is contraindicated for pregnant women. Studies have shown that isotretinoin, a known teratogen, increases the risk of miscarriage and exhibits harmful effects on the fetus. Prenatal exposure to isotretinoin may result in central nervous system abnormalities, facial dysmorphism, cleft palate, external ear malformations, parathyroid and thymus gland abnormalities[14]

In contrast to retinoids, some of the many oral antibiotics used for treating acne vulgaris are suitable for pregnant individuals, among which penicillin agents, cephalosporins and macrolide agents are especially suggested by experts.[6,16] Throughout all stages of pregnancy, penicillin and cephalexin are deemed safe for use. On the other hand, research findings on amoxicillin are inconclusive. Amoxicillin, while generally considered safe, has been associated with a potential risk of cleft lip and cleft palate when used in the first trimester.[4,6,27,28] Considering this, it is advisable to limit the use of amoxicillin to the others trimesters.[4] The administration of oral erythromycin, a representative of macrolide agents, is perceived to be safe for treating moderate to severe inflammatory acne at any trimester of pregnancy when used for a limited period of time (a few weeks).[9,29] Caution is advised in prolonged treatment decisions, as its extended use beyond six weeks has not been studied.[9] For patients who do not respond to or cannot tolerate erythromycin, azithromycin serves as an alternative macrolide, albeit with less safety data available.[4] Once macrolides and penicillins/cephalosporins are deemed to be ineffective, clindamycin can be prescribed as a next option for oral antibiotic therapy against acne as it too has been found safe in pregnant individuals. On the other hand,

several other oral antibiotics commonly administered for the treatment of *acne vulgaris* are basically advised against during pregnancy, and their use, if any, is allowed only in very special circumstances. For instance, experts recommend avoiding tetracyclines after the 15th week of pregnancy due to the potential risks of teeth discoloration and bone growth inhibition, yet consideration of their use may be warranted during the first trimester.[16] It is crucial to note that prescribing oral antibiotics during pregnancy should be reserved for situations with a clear and justified need. Moreover, to address the increasing prevalence of bacterial resistance, it is generally recommended to combine such therapy with topical benzoyl peroxide and minimize the duration of oral antibiotic usage as much as possible.[9]

For pregnant patients experiencing a severe form of antibiotic-resistant acne, considering a short regimen of low-dose prednisone may be also appropriate. Although, based on available research, oral prednisone is deemed safe only in the second and third trimesters, with a recommended dosage of < 20 mg/day and a maximum treatment duration of 1 month.[9]

In the context of hormonal acne another beneficial drug worth mentioning is spironolactone, an anti-androgenic agent with inhibitory effects on 5-alpha reductase.[16] However, akin to retinoids, the use of this medication is not recommended during pregnancy (due to the potential risk of hypospadias and the feminization of male fetuses).[16,30]

Table 2 summarizes the oral medications used in the treatment of acne vulgaris, along with indications of their safety during pregnancy.

Table 2. Acne treatment during pregnancy – oral medications[4,9,14,16]

Oral medications	**Safety during pregnancy**
Isotretinoin	Contraindicated in pregnancy
Penicillin	Safe in all pregnancy stages
Cephalosporins	Safe in all pregnancy stages
Macrolide agents (erythromycin, azithromycin*)	Safe in all pregnancy stages when used for a limited period of time (a few weeks)
Amoxicillin	Safe in the second and third trimester
Clindamycin	Safe in all pregnancy stages
Tetracyclines	Consideration of their use may be warranted only in first trimester

Low-dose prednisone (<20 mg/day)	Safe only in the second and third trimesters, maximum 1-month treatment duration
Spironolactone	Contraindicated in pregnancy

*azithromycin – less safety data available than in erythromycin

For medical professionals assessing the safety of drug use during pregnancy is a highly responsible and sometimes incredibly challenging task. In everyday medical practice assistance in this matter can come from several systems that rate the teratogenicity of medications, as well as up-to-date scientific reports. In the past, the most recognized and widely used classification was that of the Food and Drug Administration (FDA) on which reliance is now not recommended as it is deemed out of date. As its successor, the FDA has issued Pregnancy and Lactation Labeling Rule (PLLR). PLLR, instead of giving alphabetical classification (A, B, C, D and X) provided by its predecessor, went into the direction of allowing specialists for easier decision making based on current data analysis, through establishment of a set of rules and guidelines according to which safety of a product should be explained.[31]

Procedural interventions

Light and laser therapies, such as photodynamic therapy (PDT), narrowband-ultraviolet B phototherapy (NBUVB), neodymium-doped yttrium aluminum garnet laser (Nd:YAG laser) and pulsed-dye laser, constitute alternative options for acne treatment, even in pregnant patients without known teratogenic effects. It must be noted, though, that when using this type of treatment during pregnancy, there are also some important considerations.[4] The safety of using PDT with photosensitizing agents, such as aminolevulinic acid (ALA), during pregnancy is uncertain; therefore it is advisable to avoid combining PDT with ALA in pregnant individuals.[4,16,32] Moreover high cumulative doses of NBUVB may decrease folic acid levels, posing concerns for proper fetal development; thus ensuring the right supplementation is recommended.[4]

In the management of acne vulgaris during pregnancy chemical glycolic acid peels may be also considered. According to studies, such intervention can effectively address both inflammatory and comedonal acne, as well as postinflammatory lesions. Additionally glycolic acid peels enhance the cutaneous absorption of other topical agents.[9,33] Notably, no published reports indicate its negative outcomes during pregnancy.[9]

Skin care

In addition to acne treatment, proper skin care is essential for maintaining healthy skin, and pregnancy is one of the more demanding periods in this regard.[34] Ensuring adequate skin care is important not only during the active period of acne, but also when the condition is mostly clear and well-managed.[35] Selecting appropriate products is crucial. Sebum regulation, antibacterial and anti-inflammatory actions as well as

moisturizing should be the focus of acne-prone skin care. Well-chosen cosmetics should purify the skin, reduce the pathological bacterial flora residing on it, alleviate inflammation and improve the overall appearance of the skin.[36] However, reading and understanding the chemical composition of products is vital, as certain substances are not recommended during pregnancy.[34] Many dangerous chemical compounds can cross the epidermal barrier, getting further into the dermis and finally into the systemic blood circulation.[37] In general, during pregnancy it is not recommended to use cosmetics with: retinoids, high concentrations of fruit acids, hydroquinone, caffeine, trichloroacetic acid, essential oils, triclosan, fluoride, ammonia or synthetic detergents.[34,38] Hypoallergenic and alcohol-free cosmetics are preferred.[38] For facial cleansing, it is advisable to choose a non-soap cleanser with a pH close to 5.5.[39] It is strongly discouraged to use products that act aggressively on the skin and can lead to its further irritation. Moreover, acne-prone skin typically does not require additional oiling; instead, it benefits more from effective moisturization.[36] Another important aspect is proper photoprotection, as sun exposure may trigger or exacerbate acne, and contribute to the formation of comedones.[39]

Diet

Recent studies concluded a connection between the diet and the intensity of acne, even though the debate about the actual correlation has been ongoing for years.[23] Adherence to a certain diet is associated with lipid metabolism, carbohydrate metabolism, and hormonal balance, as well as with the regulation of the gut microbiome and the presence of inflammation. Some studies suggest a higher prevalence of acne among individuals who follow the so-called Western diet, which is characterized by a high intake of carbohydrates with a high glycemic index, dairy products, nuts, and chocolate, while being low in polyunsaturated fatty acids.[40] Following a high-glycemic diet requires increased insulin production to maintain normal glucose levels, and frequently results in insulin resistance, which could modify sebum production, consequently contributing to the development of acne.[40,41] On the other hand, protective effects against acne are also attributed to unsaturated fatty acids, fruits, and vegetables.[23] Another intriguing aspect of the diet-acne nexus is the role of increased milk intake in the development of new acne lesions. The results of past studies have repeatedly been controversial, but a meta-analysis by M. Aghsi and al. found a positive correlation between the intake of dairy products, including total milk, whole milk, low-fat milk, and skim milk, and the acne occurrence.[42] Additionally, it is worth noting that people with acne have been found to have lower concentrations of certain elements and vitamins, presumably whose deficiency may affect the skin condition. Among the vitamins that affect the condition of the skin are vitamin A, D and E.[40] However, special care should be taken, remembering that excess vitamin A in pregnant women can cause teratogenic effects.[43] An essential element in the context of acne is zinc, which possesses antibacterial, anti-inflammatory and anti-seborrheic effects. The recommended dietary zinc intake for pregnant individuals is set at 11 milligrams per day.[9]

Physical activity

Attitudes toward physical activity in pregnant women have evolved over the years. According to research, engaging in moderate physical activity during an uncomplicated pregnancy offers various benefits for maternal health.[44] Among these advantages is enhanced blood circulation and skin oxygenation, which in turn improves the condition and appearance of the skin. Nonetheless, during intense workouts a significant amount of sweat and sebum is secreted, which combine with impurities on the skin. This condition can cause clogged pores, consequently promoting inflammatory processes. Therefore, it is important to remove makeup before engaging in physical activity and adhere to proper hygiene practices.[45]

Psychological suport

In the clinical management of acne in pregnant patients, it is crucial for healthcare providers to consider the psychosocial impacts of the condition.[6] The literature indicates a higher incidence of depression and suicidal ideation among individuals receiving acne treatment.[46] Furthermore, patients often face additional social challenges, which may include difficulties with social interaction and public engagements, concerns about sexual attractiveness, strained relationships with family and friends, experiences of negative judgment and stigmatization, elevated stress levels, and fears regarding scarring or the chronicity of the disease. Stress plays a significant role in the context of acne, demonstrating a mutual pathophysiological link to its susceptibility and severity. This means that not only can stress increase the risk and worsen the manifestation of acne, but the presence of acne can also lead to heightened stress levels in individuals. Furthermore, stress-related behaviors, such as "skin scratching," can lead to additional adverse acne outcomes including inflammation, scarring, discoloration, and exacerbation of concerns regarding one's appearance.[39] It is also worth noting that pregnancy itself is a period of the so-called "psychological crisis", with the most critical phases being the first and third trimesters.[47] In light of the psychological challenges during pregnancy, especially in relation to acne, it is essential to offer a holistic model of maternal care that incorporates both dermatological treatment and psychological support. To address these psychological needs, various support groups for acne sufferers are available, providing a community for sharing experiences, access to educational resources, and support through telephone helplines.

In light of the aforementioned, it is worth considering a comprehensive approach to managing acne vulgaris during pregnancy, which, in addition to pharmacological treatment, includes the use of procedural interventions, an appropriate skin care and diet, physical activity, as well as psychological support (Fig. 1).

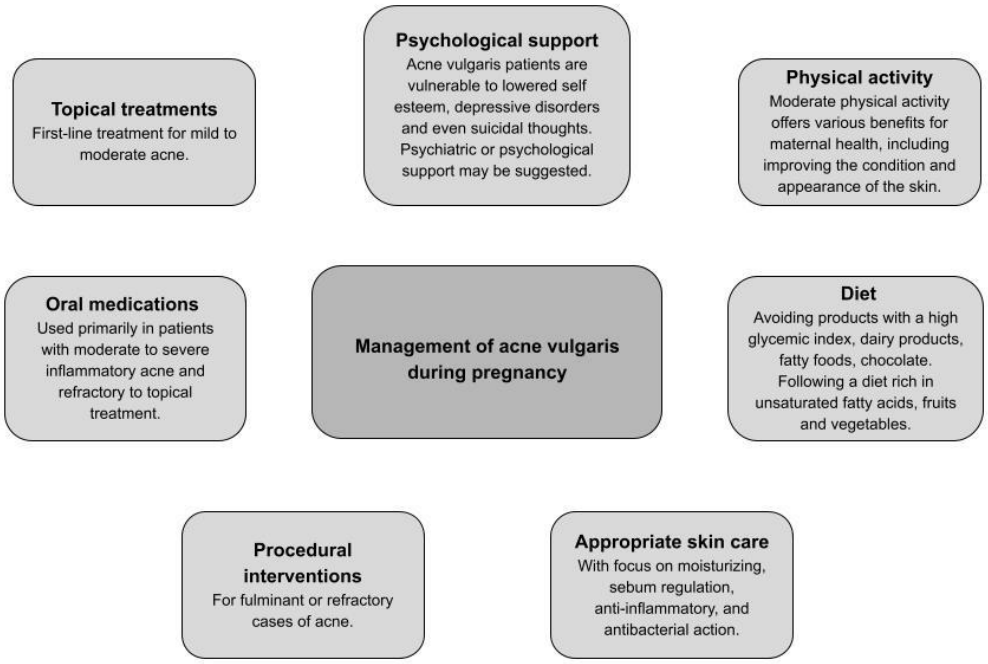

Fig. 1. Acne vulgaris during pregnancy comprehensive approach[4,9,23,26]

Conclusion

Management of acne vulgaris in pregnant women can be challenging, but when effectively conducted, it not only eliminates the physical symptoms of the disease on the skin, but may also contribute to improving the mental well-being of patients and their ability to function in daily life. Naturally, many issues in that matter are still uncertain, and there are bound to be many new research results that may clear up doubts. Medicine is a dynamically changing science, so it makes sense to revisit the same issues repeatedly and update the state of knowledge based on the most recent research. Nevertheless, when it comes to managing acne during gestation, the prevailing consensus across various studies underscores the paramount importance of prioritizing safety for both the mother and the developing fetus, and it is crucial to always bear this in mind.

Declarations

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Author contributions

Conceptualization, D.M., M.B. and J.K.; Resources, J.K., D.M., M.B. and U.G.; Writing – Original Draft Preparation, J.K., D.M. and M.B..; Writing – Review & Editing, J.K., D.M., M.B., U.G., A.U., A.R.C. and F.C.; Visualization, J.K., D.M. and A.U.; Supervision, J.K.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

Not applicable.

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