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Implications of Antimicrobial Resistance during Acne Treatment: Review Article

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ABSTRACT

Background: P. acnes is a pleomorphic rod that is aerotolerant, anaerobic, Gram positive, non-spore-forming, and a member of the class Propionibacteriales in the phylum Actinobacteria. Antibiotic therapy for acne is widely recognized as an effective strategy for managing this common skin condition. P. acnes skin colonization can also lead to Pseudomonas folliculitis, a Gram-negative folliculitis. By stimulating a regional upsurge in keratinocyte autophagic activity, P. acnes strains may play a role in antimicrobial defence pathways.

Objective: This review article aimed to assess the antimicrobial resistance during acne treatment.

Methods: We searched PubMed, Google Scholar, and Science Direct for information on Antimicrobial Resistance with Acne Treatment. However, only the most current or comprehensive study from January 2000 to May 2021 was considered. The authors also assessed references from pertinent literature. Documents in languages other than English have been disregarded since there aren't enough resources for translation. Unpublished manuscripts, oral presentations, conference abstracts, and dissertations were examples of papers that weren't considered to be serious scientific research.

Conclusion: Antibiotic resistance in P. acnes could compromise the success of acne treatments. Extensive use of antibiotics to treat acne may have consequences in other illnesses where P. acnes may be the etiological culprit. Recent research has shown that the phylotype IA1 is the most common among resistant strains. Variants of this genotype that are resistant to antibiotics have been discovered all over the world, including on the skin of otherwise healthy people.

Keywords: Antimicrobial Resistance, Acne Treatment.

INTRODUCTION

In normal skin, the cutaneous microbiome is in a delicate balance that can be thrown off by external factors, potentially leading to a number of inflammatory skin illnesses. Corynebacteria, Propionibacteria, and Staphylococci are the top three genera of cutaneous bacteria **(1).**

Structure of P. Acnes:

Acne-causing, Propionibacterium acnes is a commensal of human skin that is Gram-positive, does not form spores, and thrives in anaerobic environments **(2)**. Like Propionibacterium avidum, Propionibacterium granulosum, and Propionibacterium humerusii, it is part of the typical skin microbiota. The entire P. acnes genome, at a size of 2.5 Mb has been sequenced. Lipases that degrade pilosebaceous follicle lipids give the bacteria energy, and the genes that code for these enzymes allow the bacterium to survive in microaerophilic conditions **(3).**

After the discovery of the lipase genes triacylglycerol lipase and lysophospholipase, which are specific to the breakdown of sebum lipids, a proposal was made to rename P. acnes to Cutibacterium acnes in order to reflect the genomic adaptation changes and to differentiate it from other Propionibacteria species **(4)**.

Some have advocated, however, that the name should be changed back to "Cutibacterium acnes" for a number of reasons, including the potential for misunderstanding with the old name. As far as taxonomy is concerned, it is acceptable to keep calling the cutaneous group Propionibacterium within the field of dermatology **(5).**

Microbiology of P. Acnes:

P. acnes is a pleomorphic rod that is aerotolerant, anaerobic, Gram positive, non-spore-forming, and a member of the class Propionibacteriales in the phylum Actinobacteria. This bacterium is nonpathogenic and is found as a component of the normal flora of the skin, mouth and digestive and urine systems. Rather of flourishing in an acidic or alkaline environment, P. acnes thrives in the more neutral pH range of 6.0 to 7.0. Aerobic blood culture bottles are ideal for P. acnes because they lack the anaerobic microenvironment that occurs at the bottom of nonshaken bottles. The optimal growth temperature lies between 30 and 37 degrees Celsius **(6).**

Acne pathology can't start until P. acnes has colonized the skin, but that's not enough on its own. Patients with acne have P. acnes make up more than 30% of the face microbiota, and this bacterium is present in 87% of clones in both acne and non-acne patients **(7).**

Conversely, P. acnes may reduce the expansion of S. aureus and S. pyogenes by boosting triglyceride hydrolysis and propionic acid generation. The pilosebaceous follicle, as a result, has a constantly acidic pH. Damage to the skin's protective barrier and inflammation could result from a shift in the microbiome's composition **(8).**

Acne is associated with a different phenotype of P. acnes, and distinguishing phylotypes in patients with

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acne from those without is possible. In cutaneous samples, P. acnes was observed to be absent in the presence of Pseudomonas species and vice versa [4].

Infection with the Gram-negative bacterium Pseudomonas folliculitis has been connected to the use of antibiotics for acne. Because P. acnes strains can locally increase autophagic activity in keratinocytes, they might contribute to antimicrobial defence pathways [9]. Bacteria from the skin can be collected using a variety of techniques, including swabs, scrapes, cyanoacrylate gel biopsies, and needle biopsies. Various anatomical components and areas of skin are the focus of each method. Bacterial populations both above and below the stratum corneum are easily sampled [7]. It is difficult to obtain an accurate hair follicle sample since bacteria may be located further down in the hair follicle, a skin biopsy may be required [10].

Biofilms could be a form of bacterial existence in their native environments. Biofilms are characterised as microbial aggregates encased in extracellular matrix that shield cells from abiotic stresses and help them evade the host immune system. If P. acnes biofilm is able to penetrate into sebum and function as an adhesive, then corneocytes may become more cohesive and microcomedones may be formed [11]. In addition, compared to control samples, P. acnes from acne samples are more likely to develop biofilms in the sebaceous follicles [4].

Acne vulgaris is caused by a bacterial species called Staphylococcus epidermidis (S. epidermidis), in addition to Propionibacterium acnes. The combination of S. epidermidis and P. acnes leads to biofilm formation, which in turn inhibits hair follicles and pores and creates an anaerobic environment under the skin, further encouraging bacterial growth and making it more difficult to cure the acne [12].

P. Acnes Response to Antibiotics:

The prevalence of P. acnes strains resistant to at least one antibiotic has increased dramatically during the past three decades, from 20% in 1979 to 64% in 2000. Tetracycline resistance was significantly lower than clindamycin and erythromycin resistance. A survey of 664 people in the UK, Spain, Italy, Greece, Sweden, and Hungary found that 50.8% to 93.6% of those affected by P. acnes were resistant to at least one of four classes of antibiotics: tetracycline, macrolide, lincosamide, or streptogramin B [1].

Antibiotic resistance among P. acnes strains differs internationally, according to in vitro tests. The difference could be attributed to regional variations in antibiotic prescribing practices and concomitant topical medication use. In studies including patients with acne in Korea, the United Kingdom, Colombia, Mexico, Hong Kong, Hungary, and Spain, antibiotic resistance in P. acnes was discovered in 36.7%, 55.5%, 40.7%, 75.5%, 54.75 %, 51.5%, and 94 %, respectively [9].

Macrolide-resistant Acne vulgaris patients are a common source for isolating P. acnes, and the majority of resistant isolates carry the 23S rRNA mutation. P. acnes developed resistance after being exposed to macrolides for an extended period of time at sub-therapeutic concentrations [8].

Implications of Antimicrobial Resistance:

Antibiotic-resistant P. acnes has the potential to diminish the effectiveness of acne therapies. Possible implications in acne and other disorders where P. acnes may be the causative pathogen due to widespread use of antibiotics for acne treatment may lead to the emergence of strains of P. acnes with cross-resistance to different antibiotics [9].

Recent research has shown that the IA1 phylotype is predominately where resistant bacteria can be found. Variants of this genotype that are resistant to antibiotics have been discovered all over the world, including on the skin of otherwise healthy people [13].

Considering the widespread use of antibiotics to treat acne, current treatment recommendations seek to reduce the likelihood that P. acnes and other bacteria will develop resistance to these drugs. Avoid using topical antibiotics as monotherapy for extended periods of time because this practice may contribute to the development of antibiotic-resistant P. acnes. Acne that is mostly comedonal should not be treated with antibiotics [14].

In cases with papulopustular, inflammatory face acne, a topical antibiotic may be recommended, especially when used in a fixed combination with benzyl peroxide (BPO) or retinoid. Advantages of topical fixed-dose combination treatments include a more rapid onset of action and possibly less antimicrobial resistance than is seen with antibiotic monotherapy. To lessen the likelihood of bacteria developing resistance to topical antibiotics, adding either benzoyl peroxide or a topical retinoid is recommended [4].

Maintenance acne treatment should not involve the use of antibiotic creams instead, retinoids should be applied topically, with BPO added for antibacterial impact if necessary. In addition, BPO inhibits the growth of P. acnes, making it an effective antimicrobial. Protein synthesis can be inhibited by azelaic acid without generating bacterial resistance in aerobic or anaerobic microorganisms, including P. acnes [9].

Systemic antibiotics in addition to a topical treatment may be useful for treating mild to severe inflammatory papulopustular acne and acne that affects the trunk (benzoyl peroxide, retinoid, or azelaic acid). There should be no more than a three-month break between courses of oral antibiotics. Tetracyclines (doxycycline or lymecycline) administered orally are the first to be investigated when a systemic antibiotic is sought for acne. As P. acnes has been shown to exhibit widespread antibiotic resistance, oral macrolide therapy is not a good option for its treatment [14].

Although oral isotretinoin is not an antibiotic, it has been linked to a decrease in the number of P. acnes

isolates cultured from the cheeks but had no effect on P. acnes samples taken from other anatomic regions, as has been the finding of many studies involving patients with cystic or severe acne vulgaris treated with oral isotretinoin [(1)].

Topical photodynamic treatment (PDT) employing photoactivation of aminolaevulinic acid (ALA) or methyl aminolaevulinate (MAL) is one of the new off-label therapeutic approaches for acne that focuses on P. acnes, demonstrating the significance of this bacteria in the pathogenesis of acne. PDT's mechanism of action includes photodynamic damage to the sebaceous gland and photodestruction of P. acnes [(9)].

Studies into the possibility of a vaccination against P. acnes were halted in 2011 after showing no evidence of benefit in humans with acne. In ex vivo models of acne, antibodies against the Christie-Atkins-Munch-Peterson (CAMP) factor have been demonstrated to be beneficial at dampening the inflammatory response. Incubating ex vivo acne skin explants with monoclonal antibodies (mAbs) directed against P. acnes-secreted CAMP factor reduced the levels of pro-inflammatory IL-8 and IL-1. It was suggested that injecting a monoclonal antibody against CAMP factor directly into active lesions could be an effective treatment for acne [(4)].

CONCLUSION

Antibiotic resistance in P. acnes could compromise the success of acne treatments. The widespread use of antibiotics to treat acne has the potential to affect other illnesses where P. acnes may be the causative pathogen, as it may promote the development of strains with resistance to several antibiotic classes. Recent research has shown that the IA1 phylotype is predominately where resistant bacteria can be found. Variants of this genotype that are resistant to antibiotics have been discovered all over the world, including on the skin of otherwise healthy people.

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