

Ozenoxacin: A Review of Clinical Efficacy on Impetigo Treatment

Daniela Guerrero Carrillo ¹, Alejandra Guerrero Carrillo ²

¹ISSSTE Dr Santiago Ramón y Cajal

²Hospital Materno Infantil Durango

ABSTRACT

Impetigo, a common bacterial skin infection primarily affecting children, presents a global prevalence of 11.2%, with higher rates among children aged 2-5 years. Caused mainly by *Staphylococcus aureus* and *Streptococcus pyogenes*, impetigo lesions typically appear on the face, neck, and hands, spreading easily through scratching and close contact. Effective disease control is essential to alleviate symptoms, prevent complications such as rheumatic heart disease, and reduce transmission rates. Treatment with antimicrobial agents, especially topical antibiotics, is recommended for localized impetigo. Oral antibiotics are reserved for extensive or systemic infections and outbreaks. However, the emergence of antibiotic-resistant strains, including methicillin-resistant *S. aureus* (MRSA), poses a significant challenge. There is a pressing need for alternative antimicrobial agents effective against resistant strains. Ozenoxacin, a new topical quinolone, inhibits DNA gyrase and topoisomerase IV, essential enzymes for bacterial DNA replication. Unlike other quinolones, ozenoxacin effectively inhibits both enzymes at low concentrations, penetrating bacterial cells rapidly and achieving high intrabacterial concentrations. In tests against *S. aureus* and *S. pyogenes*, ozenoxacin exhibited superior bactericidal activity compared to mupirocin and fusidic acid, achieving a 3-log reduction in colony-forming units within 4 hours. Clinical studies have demonstrated the efficacy and safety of ozenoxacin 1% cream in treating impetigo, with placebo-controlled trials confirming its therapeutic effectiveness. Ozenoxacin holds promise as a valuable addition to the armamentarium against impetigo, particularly in the face of rising antibiotic resistance.

KEYWORDS: impetigo, therapy, ozenoxacin

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INTRODUCTION

Impetigo is a prevalent bacterial skin illness in children, especially those between the ages of two and five. The worldwide median prevalence of impetigo in the general population is 11.2%. However, it is 2.5 times higher in children (12.3%) compared to adults (4.9%). This indicates a significant burden of the disease, particularly for children living in low and low-middle income countries or in socioeconomically disadvantaged areas of high-income countries ¹⁻³.

Impetigo lesions commonly appear on the face, neck, and hands. However, if the itchy sores are scratched, the illness can spread to other areas of the body and to those in close contact. The primary etiological agents responsible for

impetigo are *Staphylococcus aureus* and *Streptococcus pyogenes*, both of which induce the non-bullous type, accounting for around 70% of cases. Bullous impetigo is produced only by *S. aureus* as a result of the generation of exfoliative toxins ^{4,5}.

The highly transmissible nature of impetigo poses a significant problem for educational institutions and child care facilities. In order to minimize the transmission of illness, it is advised that children remain at home for a period of 24 hours following the commencement of suitable antibiotic treatment. Effective disease control is crucial for alleviating symptoms such as itching and blisters, reducing scarring caused by scratching, and preventing uncommon yet severe consequences including rheumatic heart

disease or glomerulonephritis ⁶.



Figure 1. Skin lesions in impetigo

Treating impetigo with antimicrobial agents can quickly alleviate symptoms, hence reducing the likelihood of spreading the infection from one person to another. Clinical practice guidelines advocate the utilization of topical antibacterial agents to treat localized impetigo. They also recommend the administration of oral antibiotics for patients with extensive lesions that do not respond to topical therapy, for those with systemic infection, and for managing outbreaks that affect multiple individuals. Topical antibacterial therapy administers a concentrated amount of medication directly to affected regions of the skin, enhancing the ability of the antimicrobial to combat bacterial resistance. In addition, topical medicines have little absorption, which effectively prevents the occurrence of systemic adverse effects commonly associated with oral medications. Studies have demonstrated that topical treatment is as successful as, or even more effective than, oral medication in the treatment of impetigo ⁷.

There is a growing number of Gram-positive bacteria, particularly *S. aureus*, that have become resistant to topical

antimicrobial drugs often employed in clinical settings. Antimicrobial resistance, namely the presence of methicillin-resistant *S. aureus* (MRSA) strains, is a significant global issue. The rise of community-acquired MRSA infections has facilitated the dissemination of these resistant strains. The emergence of fusidic acid resistance in *S. aureus* has been seen in many countries, which has the potential to restrict its overall effectiveness. Resistance to the often employed topical drug mupirocin has also been documented. A recent extensive research of *S. aureus* isolates (n = 358) obtained from samples of skin and soft tissue infections in a mostly outpatient pediatric population revealed that 31.3% of the isolates exhibited resistance to mupirocin. The rising prevalence of antibiotic resistance is a significant problem for patients with empirically treated illnesses like impetigo. In such cases, therapy is typically administered without the use of microbial culture and susceptibility testing, which are crucial in determining the most effective care. There is a definite need for newer antimicrobial medicines that have alternative ways of working compared to present

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treatments for impetigo. These agents should also be effective against isolates that are resistant to existing drugs ⁸.



Figure 2. Nasal impetigo

Quinolones function by suppressing the activities of DNA gyrase and topoisomerase IV, two enzymes that play a crucial role in the production of bacterial DNA. DNA gyrase is responsible for the induction of negative supercoiling in DNA, which is crucial for DNA replication, transcription, and chromosomal structure [Citation29]. Topoisomerase IV primarily functions to separate the two daughter molecules of DNA following replication, a process known as decatenation [Citation30]. Both enzymes, DNA gyrase and topoisomerase IV, are composed of four subunits. DNA gyrase consists of two A subunits (GyrA, encoded by the *gyrA* gene) and two B subunits (GyrB, encoded by the *gyrB* gene). Topoisomerase IV also has two A subunits (ParC or GrlA, the latter in *S. aureus*, encoded by the *parC* or *grlA* genes) and two B subunits (ParE or GrlB, the latter in *S. aureus*, encoded by the *parE* or *grlB* genes) [Citation28]. Quinolones such as levofloxacin and ciprofloxacin have a greater affinity for inhibiting topoisomerase IV compared to DNA gyrase ⁹.

Ozenoxacin has demonstrated the ability to concurrently hinder the supercoiling activity of DNA gyrase and the decatenation of topoisomerase IV at the lowest doses in *S. aureus* SA113, as compared to other quinolones. The significant inhibitory activity of ozenoxacin at low concentrations can be attributed to its rapid penetration into bacterial cells within the first minute of exposure and its high

intrabacterial concentrations, which are higher than those of other quinolones in all tested microorganisms, including *S. aureus* and *S. pyogenes*, the causative agents of impetigo. The significant buildup of ozenoxacin within the Gram-positive bacterial cell may indicate its resistance to the effects of certain efflux pumps that impact other quinolones ¹⁰.

The bactericidal efficacy of ozenoxacin against *S. aureus* and *S. pyogenes*, when compared to mupirocin and fusidic acid, was proven in tests using death curves. Ozenoxacin at a concentration of two times the minimum inhibitory concentration (MIC) exhibited bactericidal activity against *S. aureus*. This was demonstrated by a 3-log reduction in colony-forming units (CFU) after 4 hours. In contrast, mupirocin and fusidic acid at concentrations equivalent to 32 times the MIC only showed bacteriostatic activity after 24 hours.

Therapeutic effectiveness

The effectiveness and safety of ozenoxacin 1% cream in treating impetigo have been proven in two important placebo-controlled phase III clinical studies. In all experiments, the placebo was a cream carrier that did not include the active component ozenoxacin. The vehicle includes benzoic acid along with other excipients ¹¹.

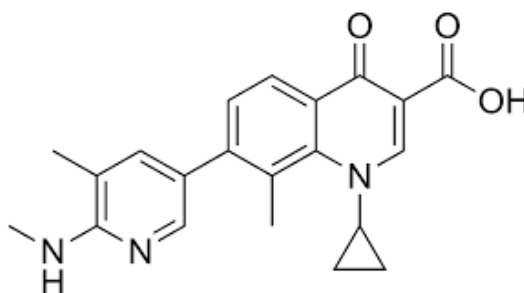


Figure 3. Ozenoxacin structure

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CONCLUSION

The capacity to manage infectious illnesses is under grave jeopardy as a result of the advent and worldwide dissemination of antibiotic resistance. The scenario is exacerbated by a concomitant decrease in the advancement of novel antibacterial drugs, significantly restricting the choices for treating progressively resistant illnesses. The development and release of a new antibiotic is a very significant occurrence. It is crucial for healthcare professionals to responsibly handle antimicrobials in order to protect their usage in the future.

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