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Opinion Article

Potential and Challenges of Phage Therapy for *Staphylococcus aureus* in Fractures

Lauren Blommer*

Department of Infectious Diseases, University of Maryland School of Medicine, Baltimore, United States of America

DESCRIPTION

Fracture-Related Infections (FRIs) pose significant challenges in orthopedic medicine, often leading to prolonged treatment, increased healthcare costs, and significant morbidity for patients. Among the various pathogens causing these infections, Staphylococcus aureus is particularly notorious due to its virulence, ability to form biofilms, and resistance to multiple antibiotics. The rise of antibiotic-resistant strains like Methicillin-Resistant *Staphylococcus aureus* (MRSA) further complicates treatment. In this context, bacteriophage therapy has emerged as a potential alternative or adjunct to traditional antibiotics. This article explores the feasibility of using bacteriophage therapy to treat *Staphylococcus aureus* FRIs, examining its mechanisms, advantages, challenges, and current state of research. Bacteriophages, or phages, are viruses that specifically infect bacteria. They have a natural ability to target and lyse bacterial cells, making them potential therapeutic agents against bacterial infections. Phage therapy involves the application of these viruses to infect and kill pathogenic bacteria. Unlike broad-spectrum antibiotics, phages are highly specific to their bacterial hosts, which allows for targeted therapy with minimal impact on the beneficial microbiota.

Phages infect bacteria by attaching to specific receptors on the bacterial surface and injecting their genetic material into the host cell. This blocks the bacterial machinery to produce new phage particles, ultimately causing the bacterial cell to lyse and release the progeny phages. This lytic cycle continues, propagating the phages and reducing the bacterial population. The specificity of phages is both an advantage and a limitation. It allows for targeted killing of pathogenic bacteria without harming beneficial microbiota, but it also means that a specific match between the phage and the bacterial strain is necessary for effective treatment. This necessitates the identification and isolation of appropriate phages for each infection.

Advantages of bacteriophage therapy for FRIs

Phage therapy offers several potential advantages in the treatment of *Staphylococcus aureus* FRIs. First, phages can target and lyse antibiotic-resistant strains of *S. aureus*, providing an alternative to antibiotics in cases of multidrug-resistant infections. Second, phages can penetrate and disrupt biofilms, which are structured communities of bacteria that are particularly resistant to antibiotics and a common cause of chronic FRIs. Additionally, phages have the ability to evolve alongside bacteria, potentially overcoming bacterial resistance mechanisms that render antibiotics ineffective. This evolutionary adaptability could provide a dynamic tool in the ongoing battle against resistant bacterial infections.

Challenges in implementing phage therapy

Despite its potential, the implementation of phage therapy faces several challenges. One of the primary obstacles is the specificity of phages, which requires the isolation and characterization of effective phages for each bacterial strain. This process can be time-consuming and may not be feasible for all infections, particularly in vital cases. Regulatory difficulties also provide significant challenges. The production and application of phages for therapeutic use require stringent quality control and regulatory approval, which can be complex given the biological nature of phages and their variability. Furthermore, the lack of standardized protocols for phage therapy complicates its integration into clinical practice. Another challenge is the potential for bacterial resistance to phages. While phages can co-evolve with bacteria, there is still a risk that bacteria may develop resistance to specific phages. This necessitates the use of phage cocktails combinations of multiple phages targeting different bacterial receptors—to minimize the risk of resistance development.

Research on phage therapy for *Staphylococcus aureus* FRIs is progressing, with several studies and clinical trials exploring its

Correspondence to: Lauren Blommer, Department of Infectious Diseases, University of Maryland School of Medicine, Baltimore, United States of America, E-mail: lauren.blommer@ihv.umaryland.edu

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efficacy and safety. Experimental studies have demonstrated the ability of phages to reduce bacterial load and biofilm formation *in vitro* and in animal models. These findings support the potential of phage therapy as an effective treatment for FRIs caused by *S. aureus*. Clinical trials are important for translating these findings into clinical practice. Several trials have been conducted or are ongoing to evaluate the safety, efficacy, and feasibility of phage therapy for bacterial infections, including those caused by *S. aureus*. For instance, a compassionate use case reported successful treatment of a multidrug-resistant *S. aureus* infection in a patient with a chronic prosthetic joint infection using phage therapy, highlighting its potential in refractory cases.

Integrating phage therapy into clinical practice for treating *S. aureus* FRIs requires a multifaceted approach. Establishing phage banks with a diverse collection of phages targeting common bacterial pathogens could facilitate rapid selection and deployment of appropriate phages for specific infections. Personalized phage therapy, according to the bacterial profile of each patient's infection, could enhance treatment efficacy and minimize the risk of resistance. Collaboration between researchers, clinicians, and regulatory agencies is essential to develop standardized protocols, ensure quality control, and navigate regulatory pathways. Education and training for healthcare providers on the use of phage therapy are also important for its effective implementation.

CONCLUSION

The feasibility of using bacteriophage therapy to treat *Staphylococcus aureus* fracture-related infections holds significant potential, particularly in the context of rising antibiotic resistance and the challenges posed by biofilm-associated infections. While there are considerable challenges to overcome, including phage specificity, regulatory difficulties, and potential resistance, ongoing research and clinical trials are providing the insights for the integration of phage therapy into clinical practice. By utilizing the natural antibacterial properties of phages, we have the potential to develop a powerful tool in the fight against persistent and resistant bacterial infections. The future of phage therapy in treating FRIs caused by *S. aureus* looks potential, offering hope for more effective and targeted treatments that can improve patient outcomes and combat the growing threat of antibiotic resistance.