INTERNATIONAL JOURNAL OF INTEGRATIVE AND MODERN MEDICINE

IJIMM, Volume 4, Issue 02, 2026 ISSN: 2995-5319
http://medicaljournals.eu/index.php/IJIMM/issue/view/3

Study of The Use of Bacteriophages in The Treatment of Purulent-Inflammatory Diseases of The Maxillofacial Region

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Abstract. Odontogenic infections range from minor abscesses to superficial and deep infections that can lead to acute infectious processes in the head and neck region and may pose a threat to the patient's life. The aim of this study is to investigate the properties of bacteriophages capable of exerting a direct effect on bacteria responsible for infections of odontogenic origin. Bacteriophages—viruses capable of destroying bacteria—were discovered in 1915; however, with the advent of antibiotics, interest in their study has significantly declined. Their use in dentistry and maxillofacial surgery remains very limited to date. The purpose of this work is to systematize literature data on the possibility of using bacteriophages as part of комплекс treatment of purulent-inflammatory diseases of the maxillofacial region, as well as to identify the main directions of research aimed at evaluating the effectiveness of this treatment complex. The presented material indicates the necessity for further studies on the use of bacteriophages as part of complex treatment in patients with odontogenic purulent-inflammatory processes of the maxillofacial region. These studies should be conducted based on the principles of evidence-based medicine, using both established and newly proposed informative tests, and should be aimed at developing experimental, clinical, and laboratory justification for their application.

Keywords: bacteriophage, maxillofacial region, purulent-inflammatory process, bacteria, complex treatment.

Introduction. Bacteriophages are a group of viruses capable of attaching to bacteria, injecting their genetic material into the bacterial cell, and ultimately inducing bacterial lysis. Their discovery dates back to the early twentieth century, and shortly thereafter their clinical application for the treatment of bacterial infections was experimentally explored. However, with the introduction and rapid development of antibiotic therapy, phage therapy was largely abandoned in Western biomedical science.

At present, humanity is approaching a post-antibiotic era, and there is an urgent need for alternative therapeutic strategies, particularly for the treatment of infections caused by multidrug-resistant (MDR) bacteria belonging to the ESKAPE group (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp.). Contemporary scientific evidence demonstrates that the emergence of antibiotic resistance among bacterial pathogens represents an increasingly serious global public health challenge.

In the coming decades, there is a significant risk that bacteria previously treatable with antibiotics will become completely resistant to these drugs. This impending threat has stimulated intensified scientific efforts in multiple directions, including the search for novel and more effective antibiotics.

At the same time, there is a growing necessity to identify alternative solutions capable of mitigating the consequences of this crisis. One such approach is bacteriophage therapy, also known as phage therapy (PT). Although this therapeutic concept originated in the early twentieth century, it has gained substantial scientific attention only in recent years. This approach is based on the use of specifically selected bacteriophages to combat pathogenic bacteria.

The activity of bacteriophages had been observed by several scientists since the late nineteenth century. However, the first scientist to recognize that this phenomenon was caused not by enzymes but by a distinct biological entity—namely bacteriophages—was the French-Canadian microbiologist Félix d'Hérelle. In 1915, during the First World War, d'Hérelle investigated a severe outbreak of hemorrhagic dysentery among French soldiers. He prepared bacteria-free filtrates from stool samples and inoculated them onto agar cultures of Shigella spp. isolated from infected soldiers. As a result, he observed clear zones, later termed "plaques." Two years later, in 1917, he presented his findings at the Academy of Sciences and proposed the term "bacteriophage," derived from the Greek word phagein, meaning "to eat," to describe the phenomenon of bacteria-destroying agents.

Recognizing the significance of his discovery, d'Hérelle conducted experiments on small animals and subsequently tested safety on himself before initiating clinical trials in humans. These efforts led to the emergence of the therapeutic approach now known as phage therapy.

Materials and Methods: Data collection was based on scientific articles and reviews published between 2010 and 2025. The primary data sources included the PubMed, Scopus, Web of Science, and Google Scholar databases, selected due to their reliability and comprehensive coverage of biomedical and biological research. In addition, supplementary sources such as other scientific journals, conference proceedings, and open-access publications were reviewed to ensure broad data coverage.

Clear inclusion criteria were established:

Clinical, laboratory, and experimental studies related to bacteriophages and phage therapy;

Research addressing odontogenic infections and purulent-inflammatory processes of the maxillofacial region;

Articles published in English and Russian;

Studies with available full-text versions.

Exclusion criteria included studies not directly related to the topic, abstracts-only publications, conference summaries without full data, duplicate publications, and studies with poor methodological quality.

Data extraction was conducted in two stages. First, titles and abstracts were screened to identify studies relevant to the topic. Second, full texts were reviewed, and relevant information—such as bacterial pathogens, phage therapy methods, application routes, efficacy outcomes, safety assessments, and clinical indications—was systematized using tables and diagrams. A descriptive analytical approach was employed to identify common trends and differences among studies.

During data analysis, comparisons were made regarding the efficacy and safety of phage therapy, administration routes (topical, oral, injectable), and clinical outcomes. Particular attention was given to the quantity and quality of existing clinical studies, and recommendations for future research were formulated. Visual tools (tables, graphs, diagrams) were used to facilitate data interpretation and analysis.

Thus, the methodology section reflects a systematic and comprehensive review of the scientific literature on phage therapy, enabling not only the synthesis of existing knowledge but also the identification of prospects for bacteriophage use in the treatment of odontogenic infections and the determination of future research directions.

Results. The simplified structure of tailed bacteriophages (class Caudoviricetes) consists of the following main components:

Head – a protein structure, typically icosahedral in shape, containing the phage's genetic material (DNA or RNA, single- or double-stranded).

Tail – a tubular structure responsible for delivering the phage genetic material into the bacterial cell.

Tail fibers or spikes – structures that recognize and bind to specific receptors on the bacterial surface, determining phage specificity.

Base plate – anchors the tail fibers and facilitates firm attachment to the bacterial surface, enabling the initiation of infection.

Bacteriophage life cycles are classified into four types: lytic, lysogenic, pseudolysogenic, and chronic. Currently, only lytic phages are considered suitable for therapeutic use in humans.

The lytic infection process proceeds as follows:

The phage attaches to the bacterial cell wall by recognizing a specific surface receptor.

Some phages produce specific enzymes (e.g., hydrolases) capable of degrading the bacterial polysaccharide capsule, exposing receptors.

Following attachment, the phage forms a pore in the cell wall and injects its genetic material into the bacterium, while the capsid remains outside.

The bacterial cellular machinery is hijacked to replicate phage proteins and nucleic acids.

Newly assembled phages accumulate, leading to bacterial lysis and release of progeny virions. The number of released phages depends on the virus type, bacterial species, and environmental conditions. After systemic administration, the primary organs involved in phage clearance are the liver and spleen, where macrophages play a key role. Animal studies have shown that phages reach their highest concentrations in the spleen, while the most rapid inactivation occurs in the liver via Kupffer cells. Renal excretion of phages is minimal due to their large size, preventing filtration through the kidneys. The administered dose, phage type, and route of administration significantly influence phage kinetics.

Several strategies exist to prolong phage circulation, including dose escalation and complement system inhibition; however, encapsulation of phage particles is considered the most promising approach. For example, Klebsiella pneumoniae–specific phages encapsulated in liposomes demonstrated prolonged persistence in the organism.

Various technological methods have been developed to enhance phage stability and shelf life, including:

Lyophilization – a two-step process involving freezing at very low temperatures followed by drying to obtain a powder suitable for inhalation.

Spray freeze drying – phage suspensions are atomized into liquid nitrogen, producing porous powder with reduced thermal stress.

Spray drying – phage suspensions are sprayed into a chamber filled with hot, dry gas, rapidly evaporating water and forming powder.

Storage at 4°C, which remains an effective preservation method.

Phage therapy is generally considered safe and is not associated with severe adverse effects. Its safety is attributed to phage specificity, as phages target only specific bacteria and do not affect the normal microbiota, unlike antibiotics. Bacterial resistance to phages develops less frequently than resistance to antibiotics.

Although phages may elicit an immune response, they do not directly affect human cells and are self-limiting in the absence of target bacteria. Numerous studies confirm the safety of phage therapy, with no serious adverse reactions reported. However, some authors note insufficient standardization in safety studies. Additionally, bacterial lysis may release endotoxins, posing a risk of toxic shock.

For instance, a case involving a 2-year-old child with MDR Pseudomonas aeruginosa sepsis and underlying DiGeorge syndrome, congenital heart disease, and antibiotic allergies demonstrated successful infection control using phage therapy, although worsening heart failure was observed.

To date, no cases of anaphylactic shock associated with phage therapy have been reported. Phage therapy has been shown to be safe in pediatric patients, although data regarding its safety during pregnancy are currently lacking.

Phage therapy requires precise matching of phages to bacterial pathogens, and phage activity in the body is relatively short-lived, necessitating the development of improved delivery methods.

Phages are commonly administered orally or intravenously, but alternative routes include inhalation, biomaterial implantation, intraperitoneal, intramuscular, subcutaneous, intranasal, tracheal, rectal, intrauterine, vaginal, and transdermal administration.

Conclusion. Before the discovery of antibiotics, bacteriophages were extensively investigated as therapeutic agents for bacterial diseases. Due to their specificity and inability to affect human cells, bacteriophages are particularly well suited for such treatments. Following the introduction of antibiotics, phage research declined in many countries. However, bacteriophages continued to be used therapeutically in countries such as Russia, Georgia, and Poland and remain in clinical use today. The increasing prevalence of antibiotic-resistant bacteria has renewed global interest in phage therapy.

The infectious nature of various dental and maxillofacial diseases—including dental caries, periodontitis, periapical lesions, oral mucosal infections, and implant-associated infections—demonstrates the potential utility of targeted bacteriophages in dentistry. Phages can disrupt or inhibit biofilm formation, reducing infection severity and enabling control of acute inflammatory stages.

Phage therapy has certain limitations, including the need for individualized treatment tailored to each patient's bacterial profile. However, this feature may also be advantageous, as therapy selectively targets the causative pathogen. Given the relative simplicity and low cost of phage isolation, further development of effective strategies to combat antibiotic resistance and support immune function is anticipated.

The resurgence of phage therapy has enabled researchers to explore this treatment modality in greater depth and develop conservative adjunctive strategies alongside conventional treatments. Consequently, there is a growing need for dentists and maxillofacial surgeons to acquire knowledge about bacteriophages.

Clinical studies indicate that bacteriophage application to purulent lesions in patients with odontogenic inflammatory diseases leads to rapid reduction of inflammatory signs and activation of reparative processes. Cytological data demonstrate enhanced leukocyte phagocytic activity following phage therapy. As a result, disease progression is more favorable in patients receiving bacteriophages, and treatment duration is shortened. Cytological indicators confirm the bacteriological and therapeutic efficacy of staphylococcal bacteriophages.

Future research will focus on conducting clinical studies to further elucidate the therapeutic effects of bacteriophages.

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