PHAGE THERAPY IN THE ERA OF MULTIDRUG RESISTANCE IN BACTERIA

Lucia GALBEN[1,2], Elena CIOBANU[1], Greta BALAN[1]

[1]*Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova
[2]*Timofei Moșneaga* Republican Clinical Hospital, Chisinau, Republic of Moldova

Corresponding author: Lucia Galben, e-mail: luciagalben@mail.ru

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Introduction. Antimicrobial resistance (AMR) is an escalating global public health threat. According to statistics from the World Health Organization, approximately 700,000 people succumb to AMR annually, and this number is expected to surge in the coming years. This statistic underscores the pressing challenges posed by AMR and the urgency to develop new, effective antimicrobial therapies. Regrettably, over the past two decades, both the U.S. Food and Drug Administration and the European Medicines Agency have only sanctioned two new antibiotic classes effective against Gram-positive pathogens but with limited impact on Gram-negative bacteria. Given that many pharmaceutical companies have ceased developing new antibiotics, meeting the pressing need for novel therapeutic agents against AMR has become increasingly difficult. With the emergence of extensively drug-resistant bacterial infections and the recognition of other limitations associated with traditional antibiotics over recent decades, bacteriophage therapy has reemerged as a strategy for treating bacterial infections. Although pharmacological antibacterial therapies overshadowed this century-old therapy in decades past, the use of lytic phages to combat infections is once again on the rise.

The aim of this study is to conduct a systematic review assessing the effectiveness and safety of phage therapy against multidrug-resistant bacteria by evaluating studies published over the past decade.

Material and methods. This systematic review evaluates the effectiveness and safety of phage therapy against multidrug-resistant bacteria by examining studies published over the past decade. To achieve this, we conducted a bibliographic search in the PubMed and Google Scholar databases. Out of the 1450 studies identified, 25 met the inclusion criteria, encompassing a total of 145 treated patients.

Results. Out of the total of 145 patients who underwent phage therapy, 128 (88.3%) experienced a reduction in or complete elimination of the bacterial load, along with an improvement in their signs and symptoms. In contrast, phage therapy was ineffective in the remaining 17 patients (11.7%). Among the patients, only 31 (21.4%) received a combination of phage therapy and antibiotics, which achieved a 100% success rate. The remaining 114 patients (78.6%) were exclusively treated with phage therapy, resulting in an 82.1% success rate. Bacterial resistance to phages was reported in 5 out of the 25 articles reviewed. In 19 clinical cases (76.0%), phage cocktails were administered, involving a combination of 2 to 12 bacteriophages, while in six cases (24.0%), a single phage was administered. The 25 cases in which phage cocktails were administered used various routes: 4 were topical (16.0%), 6 intravenous (24.0%), 5 were administered in organs or cavities (20.0%), 4 through inhalation (16.0%), and 6 cases involved more than one route of administration (24.0%).

Conclusions. This analysis demonstrates that phage therapy could serve as an alternative treatment for patients with infections linked to multidrug-resistant bacteria. Nevertheless, due to the specificity of phages required for treating various bacterial strains, this therapy necessitates personalization in terms of selecting the appropriate bacteriophage type, route of administration, and dosage.

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