Phage therapy in Belgium

Bacteriophage therapy (BT), or the therapeutical use of phages, is put forward as an additional tool against difficult-to-treat infections.
The place of phage therapy as an adjuvant of antibiotics needs to be determined with prospective studies like Phage Force(1), STAMP(2) studies and well-documented case studies and series(3) are fundamental to standardize our practices and avoid the publication biases that plague the phage therapy field today. In Belgium, dedicated and pragmatic phage therapy framework was implemented in 2018, which resulted in the facilitation (by the phage therapy coordination center at the Queen Astrid Military Hospital in Brussels) of 171 patients so far. The first 100 consecutive cases were recently analyzed, showing clinical improvement and eradication of the targeted bacteria for 77.2% and 61.3% of infections, respectively. In our dataset of 100 cases, eradication was 70% less probable when no concomitant antibiotics were used (odds ratio = 0.3; 95% confidence interval = 0.127–0.749). In vivo selection of bacteriophage resistance and in vitro bacteriophage–antibiotic synergy were documented in 43.8% (7/16 patients) and 90% (9/10) of evaluated patients, respectively. We observed a combination of antibiotic re-sensitization and reduced virulence in bacteriophage-resistant bacterial isolates that emerged during BT. Bacteriophage immune neutralization was observed in 38.5% (5/13) of screened patients. Fifteen adverse events were reported, including seven non-serious adverse drug reactions suspected to be linked to BT. While our analysis is limited by the uncontrolled nature of these data, it indicates that BT can be effective in combination with antibiotics and can inform the design of future controlled clinical trials. (4)

References

1.Onsea J, Uyttebroek S, Chen B, et al. Bacteriophage Therapy for Difficult-to-Treat Infections: The Implementation of a Multidisciplinary Phage Task Force (The PHAGEFORCE Study Protocol). Viruses. 2021 Aug 5;13(8):1543. doi: 10.3390/v13081543.

2.Khatami A, Foley DA, Warner MS, et al. Standardised treatment and monitoring protocol to assess safety and tolerability of bacteriophage therapy for adult and paediatric patients (STAMP study): protocol for an open-label, single-arm trial. BMJ Open. 2022 Dec 9;12(12):e065401. doi: 10.1136/bmjopen-2022-065401

3. Brieuc Van Nieuwenhuyse, Dimitri Van der Linden, Olga Chatzis. Bacteriophage-antibiotic combination therapy against extensively drug-resistant Pseudomonas aeruginosa infection to allow liver transplantation in a toddler. Nat Commun. 2022 Sep 29;13 (1):5725. doi 10.1038/s41467-022-33294-w

4.Djebara S, Pirnay JP et al. Personalized bacteriophage therapy outcomes for 100 consecutive cases: a multicentre, multinational, retrospective observational study. Nat Microbiol. 2024 Jun;9(6):1434-1453. doi: 10.1038/s41564-024-01705-x.