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Phage therapy review "as alternative treatment of bacterial infection"

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Abstract

The rapid increase of multidrug-resistant bacteria around the world provides an opportunity to explore phage therapy as a replacement to antibiotic usage or a complementary treatment for some bacterial diseases. A number of clinical literatures have recently documented for the results of administering bacteriophages and phage cocktails to treat various infections. Although the phage therapy has given positive results, phage therapy has not been approved or used in the clinics. The variety of phage formulations, as well as the different routes of phage administration and treatment times, make it difficult to develop such systems. In particular, the different localizations of bacterial infections make it necessary to determine the best routes of administration and treatment regimens for phages. If bacteria grow resistant to phages, phages will naturally evolve to infect the resistant bacteria, reducing the possibilities of bacterial escape, which is still another advantage of the phage over antibiotics. Because of the diminished microcirculation and the production of microbial biofilms, which are typically diverse and antibiotic resistant, antibiotic treatment of infected ulcers is sometimes hampered by low antibacterial drug bioavailability. As a result, new treatments, either as an alternative to or in addition to antibiotic therapy, are necessary. The use of lytic bacteriophages as a therapy strategy is one of the options. A simple approach of bacteriophage treatment of diabetic foot ulcers is described here.

Introduction

Since their discovery, bacteriophages have been regarded possible antibacterial treatments for the therapy of many contagious diseases' "infection" in human. At the beginning, bacteriophages were used in clinical trials to treat acute intestinal disorders and skin infections [1]. Later, bacteriophages were utilized in surgical procedure to treat purulent wounds and post-operative contaminations, and these methods were popular in the Soviet Union in 1930s and 1940s [2]. Phage therapy was phased out in most nations after the introduction of antibiotics, and surgical methods in the USSR (Union of Soviet Socialist Republic) were drastically reduced. However, in eastern part of Europe and the union of Soviet, in the clinical management of infectious wounds by using bacteriophage wasn't discontinued, since presence of antibiotic resistance bacteria create challenges to the antibiotic therapy for such infections sometimes. In Poland, Republic of Georgia and Russian Federation, phage related preparations for clinical use have been approved, and a numerous studies of bacteriophage therapy have been published in that region [3-4].

The key benefit of phages is their specificity for the target bacterium, which decreases the amount of damage to the host's regular flora. A cocktail of phages should be employed if the bacteria to be targeted cannot be identified. Bacteriophages are self-limiting, which means they need their hosts to keep growing all the time; if the bacterial pathogens they're looking for aren't there, they won't last long [5-6]. Another advantage of phages is that phage can multiply (replicate) in the infectious wound. Beside that phage are risk-free and have few or no negative effects [7-8].

Results

Phage therapy was applied in 550 cases "between" 1981-1986; it was reported that 92.4% of the patient's showed improvement, 6.9% regressed in the symptoms, and 0.7% of the patients did not experience any effect. In phage therapy applied against *Staphylococcus* and Gram-negative bacteria (*Escherichia, Pseudomonas, Proteus, Klebsiella*), which are causative agents in chronic skin infections caused by postoperative or other causes, 77% of the patients recovered, and the remaining 23% due to the development of side effects or no sign of improvement, treatment was stopped [9]. A successful phage study in the field of ophthalmology has been carried out. (Dautova et al) treated 30 patients with traumatic bacterial keratitis, 16 of whom had prulent corneal ulcers, with "Pio" bacteriophage. Patients treated with phage were discharged earlier than those treated with gentamicin, while an equal number of controls were treated with gentamicin eye drops [10]. In cancer; Phage therapy was administered to 20 cancer patients who had bacterial infection due to *S. aureus, P. aeruginosa*, *Klebsiella pneumoniae*, *Klebsiella oxytocave E. coli* and did not respond to antibiotic treatment. All patients given phage orally three times a day fully recovered between 2 and 9 weeks (mean 32 days) following treatment. 94 antibiotic-resistant septicemia cases were treated with phage, in 71 of the cases, antibiotic treatment and phage treatment were applied together, and the remaining 23 were treated with phage alone. With this treatment, 85.1% of 94 cases improved, while 14.9% had no effect [11]. The average success of phage therapy is around 80-85%, and its efficacy has been proven for combating against bacterial pathogens when the antibiotic therapy is not effective [12].

Discussion

The therapeutic use of phages is promising given the potential offered by the combined therapy of phage preparations and antibiotics, compared to monotherapy. Undoubtedly, the main challenge for the safe use of phages will be large-scale clinical trials, in accordance with the most rigorous regulatory entities. This will require the implementation of new regulations to evaluate the therapeutic efficiency of phages, which must be different from the standards established for antibiotics. Fortunately, phage therapy is now overcoming suspicions about it. Stimulated by the expected threat of a return to the pre-antibiotic dark ages, there is a major shift in the view of phage therapy and a more open attitude from government and scientific establishments. Reviews and articles on phage therapy appear more and more frequently and all this also generates a better grasp of its utilization regarding the experimental therapy, which in its current stage allows treatment for patients who have failed all the clinical options available.

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