Nebulized Bacteriophages for Prophylaxis of Experimental Ventilator-Associated Pneumonia Due to Methicillin-Resistant Staphylococcus aureus

An experimental animal study conducted in Bern, Switzerland

**Study Background**

**Ventilator Associated Pneumonia (VAP)**
- High incidence in mechanically ventilated patients and is associated with an ↑ risk of morbidity & mortality

**Methicillin-Resistant Staphylococcus aureus (MRSA)**
- Commonly isolated in VAP
- Traditional antibiotics for MRSA have poor lung penetration and limited efficacy against biofilms

**Bacteriophages in the Post-Antibiotic Era**
- Bacterial viruses "phages" have improved biofilm penetration and minimize the risk of resistance

**Study Methods and Design**

Study design: Experimental study conducted in male wistar rats

Nebulized bacteriophages
- $3 \times 10^4 \times 10$ PFU (n=10)
- $3 \times 10^4 \times 11$ PFU (n=10)

Control (n=7)

Mechanically ventilated

Inoculated with MRSA

Survival at 96 hours

**Methods: Part One**

**Step 1: Assessment of Phage Bioavailability**
- 12 animals, 3 mL of multicocktail phages via aerogene delivery to quantify phage concentration in the lungs.

**Methods: Part Two**

**Step Two: Experimental Animal Model MRSA VAP**
- Nebulized phages administered to 10 animals, 2 hours prior to ventilation. 4 hours later, animals inoculated with MRSA via endotracheal tube. Outcomes were compared to 7 uninfected/untreated animals.

**Assessment: Monitoring**
- Disease severity was assessed 3x/day over 96 hours. Score > 1 or weight ↓ by >20% classified as a "non-survivor".

**Study Outcomes**
- **Primary outcome was animal survival at 96 hours**
- Secondary outcomes: number of bacteria and phages in the lung & spleen at 96 hours or time of death.

**Study Results**

**Nebulized Phage Therapy Demonstrated a ↑ Survival Rate vs. Control**
- Animals that received bacteriophages against MRSA prior to mechanical ventilation had 60% survival and 70% vs. 0% for controls; p < 0.01.

**Lung MRSA Bacterial Load Was Lower with Phage Therapy vs. Control**
- Animals that received bacteriophage PPX had ~500x less MRSA bacterial load in the lungs compared to control. No difference was demonstrated in spleen bacterial load between the groups, p = 0.24.

**Direct Correlation Between Bacterial Load and Histopathology Score in Animals That Received Phage Prophylaxis**
- Pearson two-tailed correlation test r=0.80 between ↓ bacterial load and histopathology scoring indicating ↓ lung damage with bacteriophage prophylaxis.

**Authors Conclusion**

Proof of concept: Nebulized bacteriophages prevented death associated with MRSA VAP infections in 60 to 70% of animals and resulted in a decreased bacterial burden and lung damage.