

Use of Customized Bacteriophages in the Treatment of Chronic Nonhealing Wounds: A Prospective Study

The International Journal of Lower
Extremity Wounds
1–10

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DOI: 10.1177/1534734619881076

journals.sagepub.com/home/ijl



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Abstract

Nonhealing ulcers are a great challenge to surgeons as they may occasionally culminate in amputation of the affected part. Mostly nonhealing of wounds results due to infection by antibiotic-resistant bacteria and subsequent biofilm formation. However, customized bacteriophage therapy may take care of both of the above-mentioned hurdles. A total of 48 study subjects of age group 12 to 70 years, having minimum one eligible full-thickness wound and failed to heal in 6-week duration with conventional therapy, were included in this exploratory prospective study. Patients with systemic diseases, that is, burn, malignancy, dermatological disorders, and ulcers with leprosy or tuberculosis, were excluded. However, subjects having diabetes and hypertension were included in the study. The customized monophage for single bacterial infection and cocktail of phages specific to 2 or more infecting bacteria were applied on an alternate day over the wound surface. A total of 5 to 7 applications were made till the wound became free of infecting bacteria. The study period extended from August 2018 to May 2019. The study subjects were followed for 3 months since the start of therapy. A cure rate of 81.2% could be obtained, of which 90.5% (19/21) patients were nondiabetic and 74.1% (20/27) diabetic. The wounds infected with *Klebsiella pneumoniae* were observed with relatively delayed healing. Post phage therapy, the mean hemoglobin level and percentage of lymphocytes increased significantly. The customized local phage therapy is very promising in nonhealing ulcers.

Keywords

bacteriophage, chronic wound, diabetes, healing, biofilm

Introduction

Human skin is one of the components of innate immunity protecting against microbial invasion and maintains the body temperature and fluid homeostasis. A breach in the skin disrupts this barrier and poses many health challenges. Skin wounds often lead to local infection including gangrene and systemic sepsis.¹ Of the chronic wounds, not healing within 6 weeks are referred to as nonhealing chronic wounds.² It is estimated that approximately 1% to 2% of the world's population suffers from chronic wound during their life time.³ The significance of the chronic wound could be appreciated by a conservative estimate of the United Kingdom in the year 2005, which estimated around 3% of out-of-turn expenditure was on chronic wounds. The total cost to the National Health Services for caring the patients with chronic wounds could be estimated to be US\$3.4 to US\$4.6 billion per year.⁴ Although 2 wounds are never identical, the factors predisposing for the chronicity may be shared, that is, wound infections, biofilm, inflammatory mediators, hypoxia, poor nutrition, and

repeated trauma often due to neurological deficiency or anatomical locations.⁵ Both infection and subsequent biofilm formation are the major causes of the persistence of the wounds.^{6,7} Debridement is the pivotal step in the treatment of any form of wound.⁸ However, simple debridement has minimal effect on surface bacterial count.⁹ The application of topical antiseptics and antimicrobials usually fails to eradicate biofilm.¹⁰ Furthermore, because of poor blood supply, systemic antibiotics fail to penetrate the biofilm. The emergence of antimicrobial resistance in the microbes is an added hurdle to deal with the bacteria infecting the wound.¹¹ Several wound dressing technologies are being tried in chronic wound healing such as dressings intended for local drug delivery of antimicrobial, anti-inflammatory,

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