Therapeutic efficacy of an antibiotic-loaded nanosheet in a murine burn-wound infection model

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A B S T R A C T

Polymeric ultra-thin films (nanosheets) possess unique properties that make them suitable materials for various biomedical applications. In our previous study, we assessed the use of an antibiotic (tetracycline, TC)-loaded nanosheet (or “TC-nanosheet”) for the treatment of gastrointestinal tissue defects. The nanosheet consisted of three functional layers: layer-by-layer nanosheet as a stable platform, TC as an antimicrobial agent with autofluorescence for tracing, and a poly(vinyl acetate) nanosheet to act as a protecting layer. The TC-nanosheet has high flexibility, adhesive strength and transparency. Here, we evaluated the effectiveness of the TC-nanosheet in preventing full thickness burn-wound infections. In an in vivo study, murine dorsal skin was injured by full-thickness burns and then infected with Pseudomonas aeruginosa (P. aeruginosa), a common bacterium causing burn-associated infections. The wound site was treated either with a TC-nanosheet, TC-unloaded nanosheet or left untreated. Wound management was facilitated by the high transparency of the TC-nanosheet. The TC-nanosheet significantly improved burn-wound infection by P. aeruginosa in mice. Indeed, all mice treated with the TC-nanosheet survived, whereas the other treatment groups displayed increased rates of mortality due to bacterial infection. According to histological analyses and viable bacterial counting in the liver (bacterial translocation), the TC-nanosheets were able to prevent not only the local inflammation but also systemic inflammation. We conclude that the TC-nanosheet can act as an effective treatment for full-thickness burn-wound infection. Hence, the TC-nanosheet is a promising therapeutic tool for burn-wound management in severely burn-injured patients.

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1. Introduction

Burn injuries render the host susceptible to bacterial infection because of the large skin defects that are created. Burn-wound infection often causes systemic sepsis and severe septicemia, resulting in an increase in mortality of burn-injured patients. Therefore, appropriate burn-wound care is important to prevent wound infection and improve patient outcome. It is currently estimated that ~75% of mortality following burn injuries are related to infections, such as those caused by Pseudomonas aeruginosa (P. aeruginosa) or methicillin-resistant Staphylococcus aureus (MRSA), rather than osmotic shock and/or hypovolemia [1,2].

Complication of burn-wound infection is thus considered as a serious problem in the care of severely burn-injured patients. Currently, such patients are treated by debridement to remove as much of the source of infection as possible, combined with wound dressing and, if required, tissue grafting [3]. However, it is difficult to heal “full-thickness burns”. In general, the current standard treatment of a full-thickness burn is tissue grafting. Thus, it is important to inhibit bacterial infection until tissue grafting can be performed.

There are three main factors that must be considered when choosing a suitable dressing material for burn wounds [4]: (i) controlling infection in the wound; (ii) generating a moist environment for healing; (iii) protection of the wound area from mechanical trauma. Traditionally, cotton gauze has been used as a wound-dressing material that can protect against bacteria. Unfortunately, these dressings adhere to the wound area, causing pain and further tissue damage [5]. Various wound dressings containing antimicrobial agents or silver ions have been clinically...