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ORIGINAL ARTICLE

Characteristics comparisons of bacteremia in allogeneic and autologous hematopoietic stem cell-transplant recipients with levofloxacin prophylaxis and influence on resistant bacteria emergence

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Abstract *Background:* The aim of this study was to compare the risk factors and clinical outcomes of bacteremia in allogeneic and autologous hematopoietic stem cell transplant (allo-HSCT and auto-HSCT) recipients with levofloxacin prophylaxis during the early period after transplantation.
Methods: Characteristics of bacteremia within 45 days after transplantation between allo-HSCT and auto-HSCT recipients who received levofloxacin prophylaxis between January 2005 and December 2014 were retrospectively reviewed.
Results: Of 105 HSCT recipients included in this study, 55 (52.4%) received an allo-HSCT and 50 (47.6%) received an auto-HSCT. Twenty-five patients (23.8%) with HSCT developed 28 episodes of bacteremia. Of these 25 bacteremia patients, 15 received an allo-HSCT, while 10 received an

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auto-HSCT. The occurrence of Grade 3–4 graft-versus-host disease and longer engraftment duration were associated with bacteremia in allo- and auto-HSCT recipients ($p = 0.001$ and $p = 0.002$, respectively). Auto-HSCT recipients with bacteremia had a longer hospital stay after transplantation, while allo-HSCT recipients with bacteremia had an increased 45-day mortality rate as compared with those without bacteremia ($p = 0.014$ and $p = 0.013$, respectively). All 14 Gram-negative blood isolates in this study were resistant to fluoroquinolone.

Conclusion: Levofloxacin prophylaxis in HSCT recipients is associated with the emergence of fluoroquinolone-resistant Gram-negative bacteria. The risk factors and clinical outcomes of bacteremia differ between allo- and auto-HSCT recipients, and these differences should be taken into account when designing strategies to prevent bacteremia.

Introduction

Bacteremia is a common infectious complication in patients undergoing hematopoietic stem cell transplantation (HSCT), with an incidence that ranges from 18.6% to 43.6%, depending on study design, population, and transplantation protocol used.[1–5] When bacteremia occurs in HSCT recipients, it is associated with increased morbidity and mortality.[4,6–8] Based on evidence that antibiotic prophylaxis improves clinical outcomes in patients with neutropenia after chemotherapy, the use of prophylactic antibiotics was recommended for allogeneic and autologous HSCT (allo-HSCT and auto-HSCT) recipients.[9,10] A recent meta-analysis of HSCT recipients showed that primary prophylaxis with antibiotics reduced the incidence of bacteremia as compared with no prophylaxis.[11] Despite the clinical benefits of primary antibiotic prophylaxis in HSCT recipients, concerns remain over the possible increase in antibiotic resistance.[12–15]

In Taiwan, most centers used fluoroquinolone for bacterial prophylaxis in HSCT recipients as recommended. Previous studies on the experience of fluoroquinolone prophylaxis in HSCT recipients in Taiwan focused mostly on allo-HSCT recipients.[16–18] Information concerning fluoroquinolone prophylaxis in auto-HSCT recipients has not yet been reported. Our institution has used levofloxacin for primary bacterial prophylaxis during the neutropenic phase in auto-HSCT and allo-HSCT recipients since January 2003. Initially, we used a dose of 500 mg/day; however, based on evidence that a higher dose of levofloxacin (750 mg/day) exhibited better antibacterial activity against *Pseudomonas* spp. and similar tolerance rates as compared with a lower dose of levofloxacin (500 mg/day), we shifted to a higher dose of levofloxacin (750 mg/day) in January 2011.[19]

The purpose of this study was to compare the risk factors and clinical outcomes of patients with bacteremia according to the type of HSCT received and following levofloxacin prophylaxis after transplantation and analyze resistant patterns of blood isolates.

Methods

Study design

A retrospective chart review was conducted at the Tri-Service General Hospital, National Defense Medical Center, which is a 1700-bed teaching hospital in Taiwan. Patients ≥18 years of age that had received an allo-HSCT or auto-HSCT between January 2005 and December 2014, and had received levofloxacin for primary bacterial prophylaxis during the peritransplantation period, were included in this study. Patients who had received more than one HSCT were treated as multiple patients for the purpose of this study. The clinical characteristics, outcomes, and microbiological data of blood isolates from patients were retrieved by reviewing their medical charts. This study was approved by the Institutional Review Board of the hospital (TSGHIRB approval number: 1-103-05-015).

Transplantation environment and supportive care

All patients receiving a transplant stayed in the transplantation unit of the hospital, which consists of a specialized single room with the standard protective environment. The transplantation unit was equipped with high-efficiency particulate air filters and reverse-osmosis water systems for a clean water supply. Other protective measures in the unit included standard precautions for healthcare workers and low microbial-content diets.

The patients were implanted with a Hickman catheter before initiating the conditioning regimen for drug infusion and parental nutrition. Granulocyte colony-stimulating factor was transfused from the day of transplant until engraftment. Patients were advised to gargle with a 0.2% chlorhexidine gluconate solution twice a day from the start of conditioning chemotherapy for oral hygiene and to continue until the mucositis was resolved. The transplantation protocol for each patient was reviewed and approved by the cancer committee in our institution before the transplant.

Infection prophylaxis and management

All patients received acyclovir for antiviral prophylaxis from the start of conditioning until engraftment. Auto-HSCT recipients received oral fluconazole tablets, while allo-HSCT recipients received oral fluconazole tablets (from January 2005 to June 2011) or an oral suspension of posaconazole (from July 2011 to Dec 2014) for antifungal prophylaxis. Both allo-HSCT and auto-HSCT recipients were given oral levofloxacin for bacterial prophylaxis, at a dose of 500 mg/day from January 2005 to December 2010, and

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