



Brief report

Comparative study on the usefulness of antibacterial prophylaxis with levofloxacin in patients submitted to hematopoietic stem cell transplantation[☆]



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ABSTRACT

Background: Bacterial infection remains a frequent complication in patients receiving a hematopoietic stem cell transplantation (HSCT). However, the impact of the antibacterial prophylaxis mortality in these patients is controversial.

Patients and methods: Retrospective comparison of 2 consecutive groups of patients undergoing HSCT receiving (n = 132) or not (n = 107) antibacterial prophylaxis with levofloxacin.

Results: 41% of patients receiving prophylaxis with levofloxacin had microbiologically documented infection (MDI) with bacteremia, compared with 40% of those not receiving levofloxacin. The frequency of gram-negative bacteremia was 11 and 38%, the resistance to levofloxacin was 39 and 14%, and the mortality was 8 and 7%, respectively.

Conclusions: In our experience, the use of levofloxacin as prophylaxis in HSCT was associated with a lower frequency of gram-negative bacteremia but was not associated with a decreased rate of MDI and did not influence their outcome. In contrast, there was an increase in quinolone resistance in patients treated with levofloxacin.

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Estudio comparativo sobre la utilidad de la profilaxis antibacteriana con levofloxacino en pacientes receptores de un trasplante de progenitores hematopoyéticos

RESUMEN

Fundamento: La infección bacteriana continúa siendo una complicación frecuente en pacientes receptores de un trasplante de progenitores hematopoyéticos (TPH). No obstante, el impacto de la profilaxis antibacteriana en la mortalidad de estos pacientes es controvertido.

Pacientes y métodos: Comparación retrospectiva de 2 grupos consecutivos de receptores de TPH según recibieran (n = 132) o no (n = 107) profilaxis antibacteriana con levofloxacino.

Resultados: En el 41% de los procedimientos de TPH en los que se administró profilaxis con levofloxacino se constató infección microbiológicamente documentada (IMD) con bacteriemia, frente a un 40% de los

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que no recibieron levofloxacino. La frecuencia de bacteriemia por bacilos gramnegativos fue del 11 y del 38%, la resistencia a levofloxacino fue del 39 y del 14%, y hubo un 8 y 7% de muertes, respectivamente.

Conclusiones: En nuestra experiencia, el uso de levofloxacino se asoció a una menor frecuencia de bacteriemia por microorganismos gramnegativos, pero no se asoció a disminución en la tasa de IMD ni influyó en su evolución. En cambio, hubo un aumento de la resistencia a quinolonas en los pacientes tratados con levofloxacino.

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Introduction

Bacterial infection is a common and sometimes fatal complication in patients receiving hematopoietic stem cell transplantation (HSCT). Approximately 20–40% of these patients have an episode of bacteraemia and the delay in starting antibiotic treatment until there is microbiological evidence implies an excess mortality.^{1,2} To reduce the risk of infectious complications antimicrobial agents have been used as prophylaxis during the neutropenia phase. Quinolones have been the most commonly used antibiotics since the 1980s. Its use has been associated with a reduction in the duration of febrile neutropenia and frequency of infections.³ However, the impact of antibacterial prophylaxis on mortality from infections is controversial. Most studies have not detected a significant decrease in the same,^{2,4} except for some meta-analysis.⁵ This, together with the possibility of developing resistance,⁶ have motivated that the use of prophylaxis is only recommended in patients at high risk, defined according to the intensity and/or duration of neutropenia.^{2,7,8}

The present study was conducted to evaluate the clinical usefulness and impact on the frequency and type of infections that the use of levofloxacin has had as antibacterial prophylaxis in HSCT recipients.

Patients and methods

239 HSCT procedures were retrospectively analysed between October 2006 and October 2010 conducted in the Transplant Unit of the Institut Català d'Oncologia-Hospital Germans Trias i Pujol. Depending on the use of prophylaxis with levofloxacin, 2 consecutive groups were analysed: those who did not receive prophylaxis with levofloxacin (n=107) between October 2006 and October 2008 and those who received prophylaxis with levofloxacin (n=132) between October 2008 and October 2010 following the recommendations of the *European Conference on Infections in Leukaemia* (ECIL). Levofloxacin prophylaxis at doses of 500 mg/day, orally, began the day of admission into the HSCT unit or, in case of administration of oral busulfan in conditioning regimen, the day after completion, and maintained until the peripheral blood recovery or until the onset of fever.

The variables analysed were age, sex, general condition (ECOG), the type of blood disorder and HSCT, the source of hematopoietic progenitors, the incidence of infection and microbiologically documented infection (MDI) with bacteraemia and without it, focal nature of the same, the type of isolated microorganism, antibiotics used, resistance to levofloxacin and progression of infection.

Infection was defined as the onset of focal fever, and MDI as any infection with positive culture for one or more microorganisms. These were divided into gram-negative and gram-positive. The antibiotics used empirically in the first febrile episode were cefepime plus amikacin, imipenem plus amikacin, meropenem and others like aztreonam if allergic to beta-lactams. If there was one second febrile episode or fever persisted 72 h after initiation of the empirical antimicrobial treatment, vancomycin or teicoplanin was added, as well as amikacin if it had not been administered yet. In the case of persistent fever for more than 5 days or suspicion of

invasive fungal infection, antifungals such as caspofungin, liposomal amphotericin B, voriconazole or amphotericin B deoxycholate were used. The result of the treatment of the first infection was categorised into 3 groups: resolution, worsening with admission to the intensive care unit or death.

Statistic analysis

A descriptive analysis of demographic and clinical-microbiological variables was performed in the 2 study groups. These characteristics were compared using the chi-square test or the Fisher exact test (for categorical variables), and the Mann-Whitney *U* test or the median test (for quantitative variables). Statistical significance was considered if $p < 0.05$. Statistical analysis was performed with the SPSS® software v. 15.0 (SPSS Inc., Chicago, IL, USA).

Results

239 HSCT procedures were analysed in 226 different patients, as 13 patients were receiving 2 HSCT procedures. 132 (55%) HSCT procedures received levofloxacin prophylaxis while 107 (45%) received no prophylaxis. There were no major differences in patient characteristics, their underlying disease, types of HSCT and the source of hematopoietic progenitors between patients in each cohort (Table 1).

Table 2 contains a description of infections and MDI with and without bacteraemia, their focal nature in case of bacteraemia, the type of germ found, the antibiotics used, resistance to quinolones, as well as the progression of the first infection. 84% of patients receiving prophylaxis presented infection compared with 87% of those who did not, with a frequency of MDI of 43 and 45%, respectively. There were no statistically significant differences between groups in the site of infection in cases of bacteraemia. There were differences between the two groups in the type of antibiotic administered due to the use of different regimens of empiric treatment during the time periods covered by the study. Mainly imipenem, amikacin and teicoplanin were used in the first period, while preferably cefepime, amikacin and vancomycin were used in the second. The frequency of use and type of antifungal used were similar in both groups. The frequency of gram-negative bacteraemia in the group treated with levofloxacin was significantly lower than in the group without prophylaxis (11% vs 38%, $p < 0.001$), although a reduction of infectious-related mortality was not observed. Instead, with the use of levofloxacin it was found 39% of resistance to quinolones, whereas it was 14% in the group without prophylaxis ($p < 0.001$). Finally, regarding those patients who died, 8% had received levofloxacin compared with 7% who did not. There were no differences in the frequency of febrile episode resolution (Table 2).

Discussion

This study demonstrates that the use of antibacterial prophylaxis with levofloxacin in patients receiving a HSCT has a limited impact in terms of reducing the frequency of bacteraemia, mortality and progression of the febrile process, decreasing the rate of

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