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Trends in *Stenotrophomonas maltophilia* Bloodstream Infection in Relation to Usage Density of Cephalosporins and Carbapenems During 7 Years

To the Editor—*Stenotrophomonas maltophilia* is a nonfermentative gram-negative bacillus that causes nosocomial infections, mainly in debilitated and immunocompromised patients.^{1,2} In the last decade, this agent has emerged as an important nosocomial pathogen.^{3–5} A study conducted from 1997 to 2001, involving 18,569 isolates of nonfermentative gram-negative bacilli, found that *S. maltophilia* was the pathogen isolated third most frequently from clinical specimens.⁵ The incidence of infection due to this pathogen ranged from 3.4 to 37.7 cases per 10,000 patients discharged.² Prior exposure to antimicrobial agents, particularly β -lactam agents, increases the risk of infection due to *S. maltophilia*.³ However, the relationship between usage density of β -lactams and the incidence of infection due to *S. maltophilia* remains controversial. The aim of this study was to evaluate the effect of the usage of antipseudomonal third-generation cephalosporins, fourth-generation cephalosporins, and carbapenems on the rates of bloodstream infection caused by *S. maltophilia* during a 7-year period (1999–2006).

This study was conducted at the Hospital das Clínicas, a 945-bed tertiary care university hospital, with 12 intensive care units (ICUs) that have 120 beds, and 3 transplant units,

affiliated with the University of São Paulo, Brazil. The hospital has a policy of restriction of use of several antibiotics, including quinolones, third- and fourth-generation cephalosporins, piperacillin-tazobactam, vancomycin, teicoplanin, linezolid, carbapenems, and polymyxins. From 1999 through 2006, cases of *S. maltophilia* bloodstream infection were identified by reports from the hospital infection control committee. The data were prospectively collected by the infection control team, according to National Healthcare Safety Network definitions. Bloodstream infection rates were calculated using the number of patient-days and central line-days in the ICUs and the number of admissions in the non-ICU care areas as denominators. β -lactam use (in milligrams) from 1999 through 2006 was converted into the number of defined daily doses (DDDs) per 1,000 patient-days used in our hospital per year. A defined daily dose is the average daily dose in grams of a specific antimicrobial agent given to an average adult patient. We used the 2008 World Health Organization DDD values for imipenem (2 g), meropenem (2 g), a fourth-generation cephalosporin (cefepime; 2 g), and an antipseudomonal third-generation cephalosporin (ceftazidime; 4 g).⁶ Data were analyzed using Epi Info 6.04 software (Centers for Disease Control and Infection). The χ^2 test for linear trend was used to evaluate the trends of incidence of bloodstream infection due to *S. maltophilia* and the use of β -lactam agents (measured in DDDs) during the study period.

From January 1999 through December 2006, data from 12 ICUs, 3 transplant units (kidney, liver, and bone marrow transplant), and 5 general wards were analyzed. The total number of patients hospitalized during the period was 316,080; there were 176,219 patient-days and 124,255 central line-days recorded in the intensive care units. We identified 100 cases of *S. maltophilia* bloodstream infection; 90% of the episodes occurred in the ICUs, and 10% in the non-ICU areas. Of the 90 cases in the ICUs, 33 (36.6%) were located in the medical ICU, 30 (33.3%) in the hematology ICU, 10 (11.1%) in the transplant ICU, 8 (8.8%) in the burn ICU, 6 (6.6%) in the surgical ICU, and 3 (3.3%) in the trauma ICU.

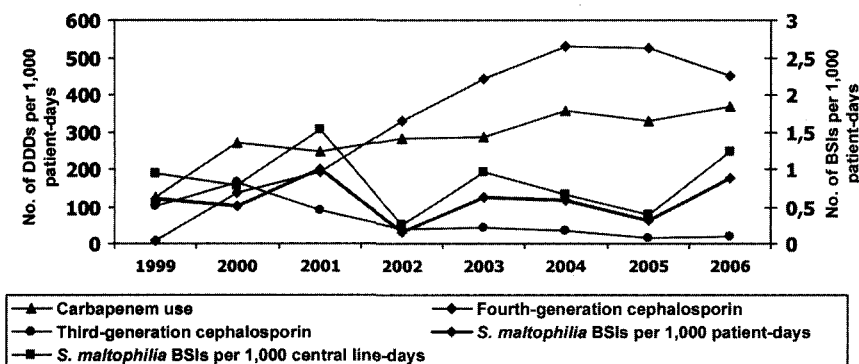


FIGURE. Comparison of median rates of bloodstream infection (BSI) due to *Stenotrophomonas maltophilia* with the use of carbapenems and third- and fourth-generation cephalosporins, in Hospital das Clínicas of the University of São Paulo, during a 7-year period. DDD, defined daily dose.

The incidence of bloodstream infection due to *S. maltophilia* did not change significantly in the intensive care units over time, ranging from 0.16 to 1.0 episode (median, 0.58 episode) per 1,000 patient-days ($P = .5$) and from 0.25 to 1.24 episodes (median, 0.84 episode) per 1,000 central line-days ($P = .1$) (Figure). In the hematology ICU and the marrow transplant units, the number of bloodstream infections due to *S. maltophilia* per 1,000 patient-days ranged from 0 to 1.6 (median, 0.7; $P = .08$).

The use of imipenem increased significantly during the study period, from 82.4 DDDs per 1,000 patient-days in 1999 to 208.4 DDDs per 1,000 patient-days in 2006 ($P < .001$). The use of meropenem also increased, from 41.2 to 160.1 DDDs per 1,000 patient-days ($P < .001$), and the use of cefepime increased from 7.8 to 449.5 DDDs per 1,000 patient-days ($P < .001$). The use of ceftazidime during the study period decreased significantly from 100.3 to 17.9 DDDs per 1,000 patient-days ($P < .001$). In the hematology unit, the use of imipenem increased from 56.8 to 152.5 DDDs per 1,000 patient-days ($P < .001$), and the use of meropenem increased from 117.4 to 428.8 DDDs per 1,000 patient-days ($P = .001$).

The effect of the use of carbapenem on rates of bloodstream infection due to *S. maltophilia* is controversial.^{7,8} Metan et al.⁸ showed, using multivariate analysis, that carbapenem use increased the incidence of *S. maltophilia* bloodstream infection. Sanyal et al.,¹ in a Kuwaiti hospital, found that the numbers of *S. maltophilia* isolates increased from 1993 to 1997, and that this change correlated significantly with an increase in the annual consumption of carbapenem. Del Toro et al.,² in a multicenter study from Spain, showed that the incidence of *S. maltophilia* infection ranged from 3.4 to 12.1 cases per 10,000 patients discharged. On the other hand, more recent studies have showed a stable incidence of *S. maltophilia* infection. Meyer et al.⁴ found that the number of *S. maltophilia* isolates at German intensive care units participating in surveillance of antimicrobial use and resistance in intensive care units did not increase from 2001 to 2004, with a mean incidence of 0.13 isolates recovered per 1,000 patient-days.⁴ According to Meyer et al.,⁴ overall antibiotic and carbapenem use increased slightly during the 4-year period.

In our hospital, bloodstream infection due to *S. maltophilia* was more frequent in the intensive care unit (90% of cases) than in non-intensive care units. Despite the significant increase in the usage density of fourth-generation cephalosporins and of carbapenems in the hospital, the rate of bloodstream infection due to this pathogen remained stable over the 7-year study period.

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Clinical Features and Treatment Outcomes of Infections Caused by *Sphingomonas paucimobilis*

To the Editor—*Sphingomonas paucimobilis* isolates have been recovered from diverse sources, including hospital water systems, respiratory therapy equipment, and various clinical specimens.¹ Several case reports and case series of *S. pauci-*