Journal of Hospital Infection 75 (2010) 23–27

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin

Impact of hospital-wide infection rate, invasive procedures use and antimicrobial consumption on bacterial resistance inside an intensive care unit

T.S. Jacoby [a,*], R.S. Kuchenbecker [b], R.P. dos Santos [b], L. Magedanz [c], P. Guzatto [c], L.B. Moreira [d,e]

[a] School of Medicine, Universidade Federal do Rio Grande do Sul, Pharmacy Department and Hospital Infection Control Committee, Hospital de Clínicas de Porto Alegre, Brazil
[b] Hospital Infection Control Committee, Hospital de Clínicas de Porto Alegre, Brazil
[c] College of Pharmacy, Universidade Federal do Rio Grande do Sul, Brazil
[d] School of Medicine and Department of Pharmacology, Universidade Federal do Rio Grande do Sul, Brazil
[e] Pharmacy and Therapeutics Committee of Hospital de Clínicas de Porto Alegre, Brazil

ARTICLE INFO

Article history:
Received 31 March 2009
Accepted 18 November 2009
Available online 24 March 2010

Keywords:
Antimicrobial use
Drug resistance
Hospital infection
Microbial resistance

SUMMARY

We performed a 30-month ecological study to determine the impact of hospital-wide antibiotic consumption, invasive procedure use and hospital-acquired infections (HAIs) on antibiotic resistance in an intensive care unit (ICU). Microbiological isolates from ICU patients with established diagnosis of hospital infection were monitored throughout the study. Overall hospital consumption per 100 patient-days of piperacillin-tazobactam, fluoroquinolones and cephalosporins increased from 1.9 to 2.3 defined daily doses (DDD) ($P < 0.01$), from 4.7 to 10.3 DDD ($P < 0.01$) and from 12.1 to 16.4 DDD ($P < 0.01$), respectively. Bacterial multiresistance in ICU was identified in 31.3% ($N = 466$) of isolates, with increasing resistance demonstrated for meropenem-resistant *Klebsiella* spp. ($P = 0.01$) and meropenem-resistant *Acinetobacter* spp. ($P = 0.02$). There was a positive correlation between multiresistance rate and DDD of cephalosporins ($P < 0.01$) and fluoroquinolones ($P = 0.03$). The rate of ceftazidime-resistant *Klebsiella* spp. correlated with DDD of fluoroquinolones and cephalosporins; the rate of ceftazidime-resistant *Pseudomonas* spp. correlated with consumption of cephalosporins, and rate of meticillin-resistant *Staphylococcus aureus* (MRSA) correlated with fluoroquinolone use. During the studied period, 36.9% ($P < 0.001$) and 34.5% ($P < 0.01$) of the changing multiresistance rate in ICU was associated with use of invasive procedures and overall HAI rate, respectively. Multiresistance rates in ICU are influenced by the variation in overall HAI rate, hospital-wide invasive procedures and antibiotic consumption outside the ICU.

Introduction

Between 5% and 15% of hospital inpatients develop an infection during hospital stay. Critically ill patients in intensive care units (ICUs) are 5–10 times more likely to acquire hospital-acquired infection (HAI) than those in non-critical wards.[1,2] HAIs are increasing in prevalence due to ageing populations, more immunocompromised patients and greater use of invasive interventions. Many of these infections are associated with multiresistant bacteria.[3–6]

Resistant micro-organisms are recognised as a reason for extended length of stay, higher costs and greater morbidity and mortality in hospital settings.[4,6,7] Previous studies suggest that there is a causal association between antimicrobial usage and antimicrobial resistance.[8,9] HAIs due to multiresistant *Acinetobacter* spp. and *Pseudomonas* spp. strains are a particular problem in ICUs of tertiary care hospitals.[10] Thus, many organisations have recommended that aggregated antibacterial drug use should be monitored at local and national levels to better understand the relationship between the use of antimicrobial drugs and emerging antimicrobial resistance.[11–13]

The present study describes the relationship between antimicrobial consumption, invasive procedures and HAIs and microbial resistance in an ICU of a teaching hospital in Southern Brazil.

Methods

Setting

The study was carried out in the adult ICU of Hospital de Clínicas de Porto Alegre (HCPA), a public, tertiary care teaching hospital in

* Corresponding author. Address: Rua Ramiro Barcelos, 2350, CEP: 90035-903, Porto Alegre – RS, Brazil. Tel.: +55 51 2101 8866; fax: +55 51 2101 8511.
E-mail address: thalita.jacoby@gmail.com (T.S. Jacoby).

0195-6701/$ – see front matter
doi:10.1016/j.jhin.2009.11.021

the city of Porto Alegre, southern Brazil. This hospital has 749 beds, with 22 non-critical wards and three ICUs (adult, neonatal and paediatric). The adult ICU has 34 beds for medical and surgical patients.

Study design and definitions

Microbiological isolates identified before or after ICU admission were evaluated. Data were reviewed for patients aged ≥15 years who had been admitted to the ICU with established diagnosis of HAI, from July 2004 to December 2006.

Bacterial isolates were reviewed from the hospital electronic database and all micro-organisms were identified by the microbiology unit. The identification of bacterial species was performed according to standard laboratory protocols and susceptibility testing by disc-diffusion method, interpreted according to Clinical and Laboratory Standards Institute guidelines.[14] Only the first microbiological isolate was considered, irrespective of the body site from which the specimen was obtained or the antimicrobial susceptibility pattern.[15] Isolates of patients with diagnosis of community-acquired infections, colonisation or surveillance data were excluded.

Hospital-acquired infections were classified by the Infection Control Committee (ICC) nurse based on diagnostic criteria of the Centers for Diseases Control and Prevention.[16] The HAI general rate was calculated by computing HAIs that occur in all critical and non-critical areas, divided by the total number of patient-days on a monthly basis.

Resistance data

Bacterial multiresistance was classified according to the CDC recommendations and ICC criteria, and included the following: extended-spectrum β-lactamase (ESBL)-producing *Klebsiella* spp. and *Escherichia coli*; ceftazidime-resistant and/or carbapenem-resistant *Pseudomonas* spp.; ampicillin/sulbactam-resistant and/or carbapenem-resistant *Acinetobacter* spp.; *Enterobacter* spp., *Citrobacter* spp., *Serratia* spp. and *Proteus* spp. resistant to all antibiotics except carbapenems; sulfamethoxazole/trimethoprim-resistant *Stenotrophomonas maltophilia*; any *Burkholderia cepacia*; vancomycin-resistant *Enterococcus* spp. and meticillin-resistant *Staphylococcus aureus* (MRSA). Isolates with intermediate susceptibility were considered resistant.[15,17]

Measures of antimicrobial use and invasive procedures

Antibiotic consumption was computed for ICU and for overall hospital (including ICU). Data on consumption of vancomycin, cephalosporins, fluoroquinolones, penicillins with β-lactamase inhibitors, carbapenems and aminoglycosides were expressed as the number of defined daily doses (DDD) per 100 patient-days on a monthly basis, as recommended by the 2005 version of the Anatomical Therapeutic Chemical (ATC) classification system and the DDD index.[18]

Information about the invasive procedures (urinary catheter and central venous catheter use, mechanical ventilation) was reviewed and classified as ICU-related and non-ICU-related. The total number of days of each of these invasive procedures was counted excluding the paediatric units (ICU, neonatal ward, and paediatric ward).

Data on antibiotic consumption and invasive procedures use were obtained from the institution's electronic database.

Statistical analysis

The bacterial multiresistance rate was calculated by dividing the number of resistant isolates for each species by the total number of bacterial isolates for each species and multiplying the quotient by 100. Linear regression was used to measure the curve trends, and Pearson's or (for non-parametric variables) Spearman's correlation coefficient (r) was used to assess the relationship between antibiotic consumption and prevalence of bacterial multiresistance. The data is reported on a quarterly basis.

A sample size of a 30 consecutive month period was estimated considering the correlation coefficient for the rate of bacterial multiresistance and antimicrobial DDD of 0.5, an α-error of 0.05 and β-error of 0.20. All collected data were stored using the Epi Info version 3.3.2 database. Data were analysed with SPSS 14.0 and STATA 10 statistical package. Statistical significance in all analyses was defined as $P < 0.05$.

The study was approved by the institution's Review and Ethics Committee.

Results

Study population

The mean ICU HAI rate from July 2004 through December 2006 was 33.3 ± 6.5 per 1000 patient-days, while the mean total hospital-wide acquired infection rate was 9.5 ± 1.0 per 1000 patient-days. The mean length of ICU stay was 5.6 ± 0.7 days; mean age of the patients in years was 58.7 ± 17.3; mean Acute Physiological Assessment and Chronic Health Evaluation (APACHE) II was 23.9 ± 9.0. Of the studied patients, 36.4% had acquired hospital infection before ICU admission.

Antibiotic consumption

From July 2004 to December 2006, the total mean antibiotic consumption for the entire hospital and ICU was 38.2 and 91.6 DDD per 100 patient-days, respectively. Total hospital consumption of piperacillin-tazobactam, fluoroquinolones and cephalosporins increased from 1.9 in the first to 2.3 DDD per 100 patient-days in the last month ($r = 0.61$, $P < 0.01$), from 4.7 in the first to 10.3 DDD per 100 patient-days in the last month ($r = 0.56$, $P < 0.01$) and from 12.1 in the first to 16.4 DDD per 100 patient-days in the last month ($r = 0.60$, $P < 0.01$) respectively. In contrast, the consumption of ampicillin-sulbactam decreased from 9.8 to 1.6 DDD per 100 patient-days ($r = -0.75$, $P < 0.01$) and aminoglycosides from 4.7 to 4.4 DDD per 100 patient-days ($r = -0.60$, $P < 0.01$) in the first and last months. No statistically significant trends were observed for carbapenem or vancomycin consumption throughout the period. Considering sole ICU antimicrobial use, only DDD of piperacillin-tazobactam and ampicillin-sulbactam changed with time, increasing from 6.8 to 9.0 DDD per 100 patient-days ($r = 0.57$, $P < 0.01$) for piperacillin-tazobactam, and decreasing from 22.0 to 3.8 DDD per 100 patient-days ($r = -0.37$, $P = 0.04$) for ampicillin-sulbactam, in the first and last months of observation.

Microbiological results

During the 30 month study period, 1490 microbiological isolates were included: 419 (28.1%) from Gram-positive bacteria [*S. aureus* (254), *Enterococcus* spp. (71), coagulase-negative staphylococci (56), *Streptococcus* spp. (24)], 866 (58.1%) from Gram-negative bacteria [*Klebsiella* spp. (179), *Pseudomonas* spp. (177), *E. coli* (126), *Acinetobacter* spp. (117), *Enterobacter* spp. (96), *Haemophilus* spp. (34), *Proteus* spp. (29), *Stenotrophomonas* spp. (28), non-identified non-fermenting Gram-negative bacilli (26), *Serratia* spp. (22), *Citrobacter* spp. (14), *Morganella morganii* (10), *B. cepacia* (5)] and 205 (13.8%) from other species [*Candida* spp. (184)]. From the 1285 bacterial isolates, 39.5% were from respiratory tract; 22.9 from