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Original Article

Antibiotic Prescriptions in Critically-Ill Patients: A Latin American Experience

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Abstract

Background: It is widely acknowledged that the presence of infection is an important outcome determinant for intensive care unit (ICU) patients. In fact, antibiotics are one of the most common therapies administered in the ICU settings. **Aim:** To evaluate the current usage of antibiotics in Latin American ICUs. **Subjects and Methods:** A one-day p-oint prevalence study to investigate the patterns of antibiotic was undertaken in 72 Latin American (LA) ICUs. Data was analyzed using the Statistix 8 statistical software, version 2.0 (USA). Results were expressed as proportions. When applicable, two tailed hypothesis testing for difference in proportions was used (Proportion Test); a *P* value of <0.05 was considered significant. **Results:** Of 704 patients admitted, 359 received antibiotic treatment on the day of the study (51%), of which 167/359 cases (46.5%) were due to hospital-acquired infections. The most frequent infection reorted was nosocomial pneumonia (74/359, 21%). Only in 264/359 patients (73.5%), cultures before starting antibiotic treatment were performed. Thirty-eight percent of the isolated microorganisms were Enterobacteriaceae extended-spectrum β-lactamase-producing, 11% methicillin-resistant *Staphylococcus aureus* and 10% carbapenems-resistant non-fermentative Gram-negatives. The antibiotics most frequently prescribed were carbapenems (125/359, 35%), alone or in combination with vancomycin or other antibiotic. There were no significant differences in the "restricted" antibiotic prescription (carbapenems, vancomycin, piperacillin–tazobactam, broad-spectrum cephalosporins, fluoroquinolones, tigecycline and linezolid) between patients with APACHE II score at the beginning of the antibiotic treatment <15 [83/114 (72.5%)] and ≥15 [179/245 (73%)] (*P* = 0.96). Only 29% of the antibiotic treatments were cultured directed (104/359). **Conclusion:** Carbapenems (alone or in combination) were the most frequently prescribed antibiotics in LA ICUs. However, the problem of carbapenem resistance in LA requires that physicians improve the use of this class of antibiotics. Our findings show that our web-based method for collection of one-day point prevalence was implemented successfully. However, based on the limitations of the model used, the results of this study must be taken with caution.

Keywords: Antibiotics, Carbapenems, Intensive care unit, Usage

Introduction

It is widely acknowledged that the presence of infection is an important outcome determinant for intensive care unit (ICU) patients, mainly due to the extremely vulnerable condition of critically ill patients and the high use of invasive procedures.[1] In fact, broad-spectrum antibiotics are one of the most common therapies administered in the ICU settings.[2]

Specific antimicrobial exposure patterns (i.e., carbapenems, broad-spectrum cephalosporins, fluoroquinolones) have been associated with the development of multidrug-resistant pathogens (MDRs) either by selecting a resistant mutant or allowing the emergence of an MDR-bacteria in a colonization flora.[3,4]

Rice recently reported these as the "ESKAPE" pathogens[5] (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae, Acinetobacter baumanii, Pseudomonas aeruginosa* and Enterobacter species) to emphasize that they currently cause the majority of world-wide hospital

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infections [Latin America (LA) included[6] and effectively "escape" the effects of antibacterial drugs].

There are several reasons for ICU specialists to choose the "best" antibiotic treatment for the seriously ill patient: infections caused by MDR bacterial strains are generally associated with increased morbidity and mortality as well as with the length of hospital stay and increased hospital cost.[7] These types of outcomes are frequently based on the well-known relationship between the inappropriate or delayed antibiotic treatment with an increase in mortality.[8]

This need for achieving appropriate therapy can lead to broad-spectrum empiric therapy (i.e., carbepenems, vancomycin, among others antibiotics), which can represent antibiotic overuse and promote even more resistance. In an effort to fight this problem, de-escalation therapy has been proposed, with the goals of reducing the number of drugs, the spectrum of therapy and the duration of therapy.[9] However, after these types of treatments are initiated, discontinuation or streamlining of the antibiotic empirical therapy based on culture results and/or clinical parameters is not the most widely practiced strategy.[10]

Based on the data described, it is well established that the evaluation of drug utilization pattern in ICU along with information on the sensitivity pattern of microorganisms from time-to-time is very crucial. Studies on drug utilization contributes to rational drug use by describing drug use patterns, detecting early signals of irrational drug use and identifying interventions to improve drug use and follow-up.

Hence, this study was carried out with the objective to evaluate the antibiotic consumption and the bacteriological profile and sensitivity pattern in LA ICUs.

Subjects and Methods

This was an observational, cross-sectional study in which 72 mixed surgical and medical LA ICUs completed a web-based data collection form, with data from the patients who received antibiotics (a one-day point prevalence done on October 11 2011).

The participating hospitals were from Argentina (n = 9), Bolivia (n = 2), Chile (n = 8), Colombia (n = 18), Costa Rica (n = 4), Ecuador (n = 14), Guatemala (n = 2), México (n = 2), Panamá (n = 1), Perú (n = 8) and Venezuela (n = 4).

ICUs were invited to participate in the web-based data collection using a unique electronic form included in the website ClinicalREC; -ATB-Terapia Intensiva Registry Program- (http://www.clinicalrec.com).

Each ICU had a principal investigator, all of whom had a personal username and password to access the electronic form.

The following data was recorded only for patients with antibiotic treatment in the ICU (prophylaxis was not included):

- General data: Type of hospital (university and non-university), number of ICU beds; number of patients admitted; number of patients admitted with antibiotic treatment, presence of infectious diseases (ID) specialist as consultant to assess the antibiotic precriptions as well as an antimicrobial optimization program at the moment of the study.
- General data of the patients: Number of registry, sex, age, date of admission in ICU, risk factors for infection due to MDR pathogens and severity of illness at admission [measured by the Acute Physiology and Chronic Health Evaluation (APACHE) II and Sepsis-Related Organ Failure Assessment (SOFA) scores].[11]
- Infection data: Date of diagnosis of infection, source of infection (community or hospital acquired); diagnosis when the antibiotic treatment was started; and microbiological documentation.
- Antibiotic use data: Severity of the disease at the beginning of the antibiotic treatment (measured by SOFA score), type of indication [(i) empirical treatment – patient with signs and symptoms of infection and cultures pendings-, (ii) culture-directed prescription – patient with signs and symptoms of infection and positive cultures, (iii) clinically documented infection – patient with signs and symptoms of infection without cultures or with negative cultures and (iv) failure with a previous antibiotic treatment]; previous antibiotic therapy during the present hospitalization (type and days of antibiotics used); antibiotic treatment of the present infection (type and days of antibiotics used); physician who prescribed the present antibiotic treatment (ICU or ID specialist) and, finally, the use of procalcitonin (PCT) test to reduce patients' exposure to antibiotics.

Established criteria were used to define clinical infection.[12]

Hospital-acquired infection (HAI) was considered that was not present or incubating in a patient at the time of admission to a hospital, but occurred within >48 h after admittance to the hospital.[12] Infections occurring within 48 h of admission to the hospital were considered community acquired, unless the patients had been transferred directly from another hospital or nursing home or discharged from a hospital within the 30 days preceding the current admission.[13]

Bacterial identification was performed according to the clinical microbiology procedures handbook.[14] Bacterial identification was confirmed, and antibiotic susceptibility testing was performed on each of the isolates using a semi-automated system in 23 hospitals (53%). In the remaining hospitals, the bacterial susceptibility was determined having used the Kirby Bauer method (disc diffusion).

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Extended-spectrum β-lactamase (ESBL)-producing microorganisms were detected and confirmed according to the standards of the Clinical Laboratory Standards Institute, using the double disc test for confirmation.[15]

For the analysis, carbapenems, vancomycin, piperacillin–tazobactam, broad-spectrum cephalosporins, fluoroquinolones, tigecycline and linezolid were considered as "restricted antibiotics" based on their epidemiological and economical implicances in the hospitals.

The study was directed in compliance with the clinical routine practices determined by the responsible physician. The study was based on a anonymous case registry methodology, and did not require the prescription of specific drugs or other treatments nor the performance of procedures or diagnostic tests other than the ones prescribed by the responsible physician. Therefore, informed consent was not required by the institutional review board from the participating institutions. The antibiotics used in the patients were the responsibility of each participant physician, justified by individual clinical circumstances and following the policies of each institution for these cases.

Statistical analysis

Data was analyzed using the Statistix 8 statistical software, version 2.0 (USA). Results are expressed as proportions. When applicable, two-tailed hypothesis testing for difference in proportions was used (Proportion Test); a P value of <0.05 was considered significant.

Results

General data

On the day of the prevalence study, there were 704 patients in the 72 participating ICUs (825 total beds), of whom 359 (51%, range between ICUs 0 and 100%) were receiving antibiotics [Table 1].

There were 47/72 (65%) ICUs in university hospitals and 25/72 (35%) ICUs in non-university hospitals. Most of the participating ICUs had an ID specialist as a consultant to assess the antibiotic precriptions [51/72 (71%)]. Only 39/72 ICUs (54%) had an ongoing antimicrobial optimization program at the moment of the study [Table 1].

Patients' median age was 57.8 years (range 18-95 years); 186/359 were male (51.8%).

The mean of the APACHE II and SOFA scores at the admission were 18 (11.8) and 7 (4.2), respectively [Table 1]. APACHE II score at admission ≥15 was observed in 245/359 patients (68%) and <15 in 114/359 patients (32%) [Table 2].

The median length of stay (LOS) was 14.9 days (range, 0-48 days).

There were 206/359 (57.4%) patients who had at least one risk factor for infection due to MDR pathogens. Previous hospitalization and previous antibiotic treatment (in both cases within the last 90 days) were the most frequent risk factors found [128/206 (62%) and 109/206 (53%), respectively] [Table 2].

Infection data

The mean of LOS since the date of ICU admission until the day of the diagnosis of infection was 11 days (range 0-34 days).

HAIs were observed in 167/359 patients (46.5%). Of all infections, 21% (74/359) were nosocomial pneumonia [52/74 (70%) ventilator-associated pneumonia (VAP)], 15% (53/359) community-acquired pneumonia, 12% (44/359) complicated intra-abdominal infection, 12% (44/359) urinary tract infection, 6.7% (24/359) central nervous system infections and 6.7% (24/359) complicated skin and skin structure infections [Table 1].

Three hundred seventy-eight samples for bacterial culture were obtained before starting antibiotic therapy in 264/359 patients [73.5% (1.43 culture/patient)]. In 52% of them (196/378), 277 microorganisms considered as the causative agent of the infection were isolated [Table 1].

We found that blood cultures (37%, 140/378) were the samples processed most frequently, in combination with respiratory secretions culture (tracheal aspirate and brochoalveolar lavage) in 33% of the patients (124/378) [Table 1].

Among isolates, ESBL-producing Enterobacteriaceae, mainly *Klebsiella pneumoniae* and *Escherichia coli* [106/277 (38%)], and *Pseudomonas aeruginosa* [48/277 (17%); 20/48 carbapenems resistant (41.5%)] were the most common microorganisms, followed by Acinetobacter spp. [42/277 (15%); 16/42 carbapenems resistant (38%)] and *Staphylococcus aureus* [30/277 (11%); 17/30 methicillin resistant (57%)] [Table 1].

Antibiotic use data

Median of SOFA score at the beginning of the antibiotic treatment was 7 (SD (4.1)).

We found that antimicrobial therapy was prescribed in the study day as empirical treatment, culture-directed prescription, clinically documented infection and failure with a previous antibiotic treatment in 50.5% (181/359), 29% (104/359), 18% (65/359) and 2.5% (65/359), respectively. At no point were the antibiotic courses discontinued, not even in cases in which cultures were not done nor in cases where the culture results were negative [Table 3].

Fifty percent of the patients (181/359) received previous antibiotic therapy during the current hospitalization [≥3 days of

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Table 1: General data of patients and institutions

Characteristics	Value
Number of participant ICU[1], *n*	72
Type of hospital, *n* (%)	
University	47 (65)
Non-university	25 (35)
ID[2] specialist as consultant in the ICU, *n* (%)	
Yes	51 (71)
No	21 (29)
Antimicrobial optimization program ongoing, *n* (%)	
Yes	39 (54)
No	33 (46)
Number of patients admitted, *n*	704
Number of patients receiving antibiotics, *n*/total (%)	359/704 (51)
Age, mean years (range)	57.8 (18-95)
Male, *n* (%)	186 (52)
APACHE II, median, *n* (%)	18
≥15	245 (68)
<15	114 (32)
LOS[3] between date of admission to the diagnostic of infection, median (range)	11 (0-34)
Origin of the infection, *n* (%)	
Nosocomial acquired	167 (46.5)
Community acquired	192 (53.5)
Type of infection, *n* (%)	
Nosocomial pneumonia[4]	74 (21)
Community-acquired pneumonia	53 (15)
Intra-abdominal infection	44 (12)
Genitourinay infection	44 (12)
Central nervous system infection	24 (6.7)
Skin and skin structures infection	24 (6.7)
Sepsis of unknown origin	24 (6.7)
Others	73 (19.9)
Cultures sites, *n* patients/total (%)	264/359 (73.5)
Cultures sites, *n* samples/*n* per patient	378/1.43
Blood cultures, *n*/total (%)	140/378 (37)
Respiratory samples[5], *n*/total (%)	124/378 (33)
Urine culture, *n*/total (%)	49/378 (13)
Peritoneal fluid, *n*/total (%)	28/378 (7.4)
Skin and soft tissue, *n*/total (%)	22/378 (5.8)
Others	15/378 (3.8)
Positives cultures	
n positive cultures/*n* total cultures (%)	196/378 (52)
Clinical isolates	
n isolates/*n* total positive cultures	277/196
ESBL[6]-producing Enterobacteriaceae, *n*/total (%)	106/277 (38)
Pseudomonas aeruginosa, *n*/total (%)	48/277 (17)
carb-R[7]-*P. aeruginosa*, *n*/total (%)	20/48 (41.5)
carb-S[8]-*P. aeruginosa*, *n*/total (%)	28/48 (58.5)
Acinetobacter spp.	42/277 (15)
carb-R[7]-Acinetobacter spp.	16/42 (38)
carb-S[8]-Acinetobacter spp.	26/42 (62)
Staphylococcus aureus	30/277 (11)
MRSA[9]	17/30 (57)
Others	51/277 (19)

[1]Intensive care unit, [2]Infectious diseases, [3]Length of stay, [4]52/74 (70%) ventilator-associated pneumonia, [5]Tracheal aspirate and bronchoalveolar lavage, [6]Extended-spectrum β-lactamases, [7]Carbapenems resistant, [8]Carbapenems susceptible, [9]Methicillin-resistant *S. aureus*

treatment in 129/181 patients (71%) and <3 days of treatment in 52/181 patients (29%)]. Broad-spectrum cephalosporins and carbapenems, followed by piperacillin–tazobactam and vancomycin (in all cases alone or in combinations with other antibiotics), were the most frequent antibiotics previously used [30% (129/181), 24.5% (44/181), 20% (36/181) and 10% (36/181), respectively] [Table 3].

During the day of the study, carbapenems (imipenem or meropenem) were the antibiotics most frequently prescribed (125/359, 35%), followed by vancomyci (91/359, 25%), broad-spectrum cephalosporins (mainly cefepime, ceftazidime and ceftriaxone) (81/359, 22.5%), piperacillin–tazobactam (66/359, 18%) and fluoroquinolones (43/359, 12%) [Table 3]. In 38% (47/125) of the cases, carbapenems were prescribed in combination with vancomycin. Carbapenems were most frequently used in culture-directed prescriptions ($P < 0.01$; data not shown).

The antibiotics used were initially prescribed in the ICU in most of the cases [287/359 (80%)]. Only a small percentage of the ICU patients continued with the treatments indicated in the emergency department, general ward and other institutions [10% (36/359), 7% (25/359) and 3% (11/359), respectively].

There were no significant differences in the "restricted" antibiotic prescription (carbapenems, vancomycin, piperacillin–tazobactam, broad-spectrum cephalosporins, fluoroquinolones, tigecycline and linezolid) between patients with APACHE II score at the beginning of the antibiotic treatment <15 [83/114 (72.5%)] and ≥15 [179/245 (73%)] ($P = 0.96$) [Table 4].

Similarly, no significant differences were found in "restricted" antibiotic prescription between university and non-university hospitals [82.5% (39/47) vs. 75% (19/25), $P = 0.07$], hospitals with or without an ID specialist as a consultant to assess the antibiotic precriptions [75% (38/51) vs. 79% (17/21), $P = 0.35$] and hospitals with or without an ongoing antimicrobial optimization program [80% (31/39) vs. 76.5% (25/33), $P = 0.60$] [Table 3].

Table 2: Risk factors for infections due to MDR[1]-pathogens[2]

Risk factor	*n/n* total (%)
Hospitalization for 2 or more days within the past 90 days	128/206 (62)
Previous antibiotic treatment within the past 90 days	109/206 (53)
Immunosuppressive illness or therapy	68/206 (33)
Hemodialysis within the past 90 days	14/206 (6.8)
Wound care at home	9/206 (4.3)
Residents of a nursing home or long-term care facility	7/206 (3.4)
Intravenous antibiotic therapy/ chemotherapy at home	5/206 (2.4)

[1]Multidrug resistant, [2]*n*=206/359 (57.4%)

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The PCT test to reduce patients' exposure to antibiotics has been used in only 16.5% of the patients (59/359), with significant differences between patients with APACHE II score <15 [11/114 (9.5%)] and ≥15 [48/245 (19.5%)] ($P = 0.02$).

Discussion

The results of this observational, cross-sectional study show that 51% of the patients admitted to a general LA ICU were receiving at least one antibiotic; in 46.5% of the cases to treat HAIs. In addition, about 60% of our patients have presented at least one risk factor for infection due to MDR bacteria; mainly hospitalization for 2 or more days and previous antibiotic treatment within the past 90 days.

It is well established that the antibiotic therapy ideally is defined by isolation of the offending organism and determination of its antibiotic susceptibility pattern.[16,17] The number of cultures obtained in our study was 73.5%, with a positive rate of 74%; nevertheless, only 29% of the patients received a culture-directed antibiotic prescription.

Prior antibiotic use is a factor that predisposes to infections with MDR-bacteria.[18] In our study, the evaluated patients received previous antibiotic treatment during the present hospitalization in 50% of the cases (71% ≥ 3 days); most of them broad-spectrum agents. In one-third of the patients, broad-spectrum cephalosporins or fluoroquinolones were used, both of which are in close relationship with the selection of MDR microorganisms; mainly, ESBL-producing Gram-negatives, the microorganisms most frequently isolated in our study.[18,19]

In terms of antibiotic prescription on the day of the study, we observed that carbapenems (imipenem or meropenem, alone or in combination with other antibiotics), were the most frequently prescribed antibiotics in LA ICUs, followed by vancomycin, broad-spectrum cephalosporins, piperacillin–tazobactam and fluoroquinolones. We have observed no significant differences in the "restricted" antibiotic prescription (carbapenems, vancomycin, piperacillin–tazobactam, broad-spectrum cephalosporins, fluoroquinolones, tigecycline and linezolid) between patients with APACHE II score at the beginning of the antibiotic treatment <15 and ≥15. In addition, considering only the prescription habit of these "restricted" antibiotics, we did not find significant differences between the indications of the ID physicians and those given by the ICU specialist. Furthermore, no significant differences were found in "restricted" antibiotic prescription between hospitals with or without an ongoing antimicrobial optimization (stewardship) program.

Although it is well established that the use of PCT improves the diagnosis of bacterial infections and to guide the antibiotic therapy,[20] less than 20% of the participant ICUs have registered the PCT use, mainly in patients with APACHE II ≥15.

Observational studies are difficult to analyze and interpret because of the lack of standardised treatment regimens and the lack of standardised indications for treatment and the lack of pre-defined endpoints. Despite the limitations, our findings show that our web-based method for collection of one-day point prevalence was implemented successfully, and has allowed to improve our knowledge on antibiotic prescription habits in LA ICUs.

Table 3: Patients antimicrobial prescription data (*n*=359)

Characteristics	Value
Type of indication, *n* (%)	
Empirical treatment	181 (50.5)
Culture-directed prescription	104 (29)
Clinically documented infection	64 (18)
Failure with a previous antibiotic treatment	10 (2.5)
Previous antibiotic therapy, *n* (%)	181 (50)
Days	
≥3 days, *n* (%)	129/181 (71)
<3 days, *n* (%)	52/181 (29)
Type	
Broad-spectrum cephalosporins*	54/181 (30)
Carbapenems (imipenem or meropenem)	44/181 (24.5)
Piperacillin-tazobactam	36/181 (20)
Vancomycin	36/181 (20)
Fluoroquinolones	25/181 (14)
Others	65/181 (36)
Patients with antibiotic in the prevalence day, *n*/total (%)	359/703 (51)
Carbapenems (imipenem or meropenem)[1]	125/359 (35)
Vancomycin[1]	91/359 (25)
Broad-spectrum cephalosporins*[1]	81/359 (22.5)
Piperacillin-tazobactam[1]	66/359 (18)
Fluoroquinolones	43/359 (12)
Ampicillin-sulbactam	40/359 (11)
Aminoglycosides[1]	38/359 (10.5)
Others	83/359 (23)

*Ceftriaxone, ceftazidime, cefepime, [1]Alone or in combination with other antibiotic/s

Table 4: "Restricted" antibotics* prescription according to patients and institution

n (%)	APACHE II[3]		Type of hospital		ID specialist[4]		AOP[5] ongoing	
	≥15 (*n*=245)	<15 (*n*=114)	University (*n*=47)	Non-university (*n*=25)	Yes (*n*=51)	No (*n*=21)	Yes (*n*=39)	No (*n*=33)
Group 1[1]	179 (73)	83 (72.5)	39 (82.5)	19 (75)	38 (75)	17 (79)	31 (80)	25 (76)
Group 2[2]	66 (27)	31 (27.5)	8 (17.5)	6 (25)	13 (25)	4 (21)	9 (20)	8 (25)
	P=0.96		*P*=0.07		*P*=0.34		*P*=0.60	

*Carbapenems, vancomycin, piperacillin-tazobactam, broad-spectrum cephalosporins, fluoroquinolones, tigecycline and linezolid, [1]Patients who received "restricted" antibiotics, [2]Patients who did not receive "restricted" antibiotics, [3]At admission, [4]Infectious diseases specialist as consultant in the intensive care unit, [5]Antibiotic optimization program

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Previously published studies show a wide range of prevalence of antibiotic use in the ICU (between 45 and 85%).[21,22] There are several reasons for the high consumption of antibiotics in the ICU: (i) patients admitted with serious community-acquired infections (i.e., community-acquired pneumonia and complicated intra-abdominal infection) and (ii) acquisition of the infection during the nosocomial stay, favored by the presence of multiple comorbidities, the high rates of invasive device use and the presence of risk factors for infections due to MDR pathogens.[23-26] In that sense, we have recently published that the prevalence of HAI in LA ICUs is 11.6%.[27]

HAI (mainly nosocomial pneumonia) accounts for nearly one-half of all antibiotic prescriptions used in our patients. In these particular indications, it is well established that the appropriate empirical antimicrobial treatment is associated with better survival; therefore, several authors recommend the use of broad-spectrum antibiotics (alone or in combination) for the empirical treatment of these serious infections.[13] However, not to consider the tailored therapy in these cases, this could lead to the possibility of "collateral damage," where overuse/misuse of antibiotics is associated with MDR-pathogen infections.[18] The low level of intention – to demonstrate the microbiology of the infections (especially in severely ill patients) – increases this possibility. The challenge is that the ICU physicians should understand that obtaining microbiological cultures before initiating empirical antimicrobial therapy is part of the diagnostic work-up of ICU patients.[27]

"ESKAPE pathogens" (with the exception of *Enterococcus faecium*) were the most common microorganisms isolated in our patients (>60%), with a similar MDR profile to that described by several microbiological surveillance systems in the region.[6,28] The T.E.S.T. program (Tigecycline Evaluation and Surveillance Trial) has found that rates of ESBL–*K. pneumoniae* and carbapenem-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa* were higher in LA than in North America and Europe (37.9%, 37.6%, 35.8% vs. 9.7%, 13.1%, 15.1% and 15.3%, 14.8%, 17.4%, respectively). In contrast, the rates of methicillin resistance among *S. aureus* were higher in North America (53.7%) than in LA (46.6%) and Europe (25.1%).[6]

The prescription habits found in our study seem justified for several reasons: (i) nearly 50% of the registered infections were nosocomial, where MDR-microorganisms are frequently involved,[29] (ii) 50% of the patients had received previous antibiotic therapy during the present hospitalization, other than carbapenems, in more than 85% of the cases. Extending the spectrum of the antibiotic previously prescribed is a very common concept between ICU physicians. (iii) High rates of ESBL-producing Gram-negatives were found in our patients. Carbapenems are stable against hydrolyzing activity of ESBLs and are regarded as the drug of choice for the treatment of infections caused by ESBL-producing Enterobacteriaceae. The combination with vancomycin extends the spectrum toward methicillin-resistant *Staphylococcus aureus* MRSA. (iv) The early effective therapy for infections in critically ill patients (defined as antimicrobial treatment that covers the infecting pathogens) is associated with low mortality rates,[30] therefore, a fresh approach to the effective treatment of patients with serious infections is to use a broad-spectrum antibacterial treatment followed by precision therapy based on susceptibility results,[8] and (v) physicians trust carbapenems because they are potent antibiotics, with an ultra-broad spectrum of activity that encompasses MDR and difficult-to-treat Gram-negative bacteria, with several clinical trial data that support its clinical effectiveness.

Although carbapenems are frequently considered the drugs of choice for treatment of serious infections due to Gram-negative organisms, there are increasing reports of carbapenem-resistant organisms worldwide. In the specific case of LA, the prevalence of carbapenem-resistant *A. baumannii* has increased markedly,[31] along with the prevalence of carbapenem-resistant strains of *P. aeruginosa*[29] and Enterobacteriaceae.[32-34] Another problem to be worry about is the description in LA of Enterobacteriaceae isolates (particularly *K. pneumoniae*) that possess carbapenem-hydrolyzing enzymes belonging to the KPC family of beta-lactamases (Colombia,[32] Brazil,[33] and Argentina[34]). Related to other classes of carbapenemases (the metallo-β-lactamases), in August 2010, reports indicated the emergence of a mechanism of resistance in enterobacteria that caused outbreaks and was related to an increase in morbidity and hospital mortality in India, Pakistan and England. Subsequently, it was also reported in Europe, Japan, Australia, Canada and the United States of America. Because of its geographical origin, the mechanism was named "New Delhi metallo-β-lactamase" (NDM).[35] In LA, the circulation of metallo-β-lactamase of type VIM had been reported mainly in non-fermenting Gram-negative bacilli, such as *Pseudomonas aeruginosa*, *Acinetobacter baumanni* and, to a smaller degree, in Enterobacteria; however, NDM had not been detected at the moment of this study. NDM-type metallo-β-lactamase has spread to different countries via the related Enterobacteriaceae as *Klebsiella pneumoniae*, an agent commonly related to hospital infections.[35] The high prevalence of carbapenem-resistant *A. baumannii* in the region has increased markedly, along with the prevalence of carbapenem-resistant strains of *P. aeruginosa* and *K. pneumoniae*.[6]

Available studies demonstrate that the interaction between the ID specialist and the attending physician may improve the diagnosis and the appropriate antibiotic treatment of severe infections.[36] Two of us (DC and RB) have found that the close interaction between the ID consultant and the ICU physician has reduced the broad-spectrum cephalosporins and vancomycin consumption significantly in the ICU, using a prospective audit of antimicrobial use strategy.[37]

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In that sense, several authors have demonstrated that ID consultation was significantly associated with an increased proportion of appropriate first-line treatments, as well as an increase in correction of first-line inappropriate treatments, when the microbiologic results become available.[36] Because antimicrobial therapy is frequently prescribed in the ICU, stewardship is particularly relevant in this setting because it provides the necessary framework to improve antimicrobial use. Our thought related to these particular findings, based on personal experience, is that the ID physicians in LA probably have the same limitations prescribing antibiotics in an ICU patient as the ICU specialist (i.e., patient′s high severity score, low percentage of microbiological documentation, misdiagnosis, "just in case" prescriptions and legal imperatives, among others).

For patients with upper and lower respiratory tract infection, post-operative infections and severe sepsis patients in the ICU, randomized-controlled trials have shown a benefit of using PCT algorithms to guide decisions about initiation and/or discontinuation of antibiotic therapy. For some other types of infections, observational studies have shown promising first results, but further intervention studies are needed before use of PCT in clinical routine can be recommended.[20] However, The limited resources frequently available in LA hospitals seems to be the main reason for the low percentage of use of this biomarker.

In conclusion, carbapenems (alone or in combination) were the most frequently used antibiotics prescribed in LA ICUs. However, the problem of the carbapenem resistance in LA requires that physicians improve the use of this class of antibiotics. In fact, the increased use of carbapenems to fight the growing prevalence of MDR bacteria, particularly ESBL-producing strains, shows early signs of eroding the effectiveness of the carbapenems. A more highly targeted and restrained use of these drugs, aimed at preserving their antimicrobial activity, is probably warranted. Their therapeutic substitution in specific pathologies is one of the strategies to reach this objective; e.g., the use of tigecycline instead of carbapenems in intra-abdominal infections where ESBL-producing Gram-negatives are suspected.[38]

However, based on the limitations of the model used, the results of this study must be taken with caution. We hope that our current study may generate enthusiasm for prospective studies, with more robust designs, in order to support or reject our conclusions.

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