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Parenteral colistin for the treatment of severe infections: a single center experience

Colistina parenteral no tratamento de infecções graves: experiência em centro único

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ABSTRACT

Objective: To describe a single center experience involving the administration of colistin to treat nosocomial infections caused by multidrug-resistant Gram-negative bacteria and identify factors associated with acute kidney injury and mortality.

Methods: This retrospective longitudinal study evaluates critically ill patients with infections caused by multidrug-resistant Gram-negative bacteria. All adult patients who required treatment with intravenous colistin (colistimethate sodium) from January to December 2008 were considered eligible for the study. Data include demographics, diagnosis, duration of treatment, presence of acute kidney injury and 30-day mortality.

Results: Colistin was used to treat an infection in 109 (13.8%) of the 789 patients admitted to the intensive care unit. The 30-day mortality observed in these patients was 71.6%. Twenty-nine patients (26.6%) presented kidney injury prior to colistin treatment, and six of these patients were able to recover kidney function even during colistin treatment. Twenty-one patients (19.2%) developed acute kidney injury while taking colistin, and 11 of these patients required dialysis. The variable independently associated with the presence of acute kidney injury was the Sequential Organ Failure Assessment at the beginning of colistin treatment (OR 1.46; 95%CI 1.20-1.79; p<0.001). The factors age (OR 1.03; 95%CI 1.00-1.05; p=0.02) and vasopressor use (OR 12.48; 95%CI 4.49-34.70; p<0.001) were associated with death in the logistic-regression model.

Conclusions: Organ dysfunction at the beginning of colistin treatment was associated with acute kidney injury. In a small group of patients, we were able to observe an improvement of kidney function during colistin treatment. Age and vasopressor use were associated with death.

Keywords: Colistin/therapeutic use; Intensive care; Cross infection/drug therapy; *Acinetobacter baumannii*; *Pseudomonas aeruginosa*; Acute kidney injury; Death

INTRODUCTION

The use of colistin to treat infections caused by resistant microorganisms is not new; clinical improvements with colistin therapy in patients with *Pseudomonas aeruginosa* infections resistant to penicillin, kanamycin and chloramphenicol were described in 1961.[1] Multidrug resistance has become increasingly common, however, and the problem continues to worsen, especially in intensive care units (ICU). *P. aeruginosa, Acinetobacter baumannii* and carbapenem-resistant *Enterobacteriaceae* pose challenges for healthcare providers around the world, including in the *Hospital Universitário da Universidade de Londrina*, where 17

cases of ventilator-associated pneumonia (VAP) caused by OXA-23 carbapenemase-producing *A. baumannii* were reported.[2] Many other outbreaks have been described;[3-5] however, controlling these outbreaks is difficult and not always successful, and these microorganisms have become endemic in many hospitals.[6-8] Many factors are associated with nosocomial infections caused by multidrug-resistant bacteria, including previous use of broad-spectrum antimicrobials, overuse of antibiotics in patients with inflammatory conditions, long-term use of empiric antibiotics, presence of invasive devices, length of stay, admission to ICU, age, septic shock, presence of comorbidities and severity of illness.[9-11]

The SENTRY study reported the susceptibility to polymyxin B in several Gram-negative bacilli between 2001 and 2004. The sensitivity to imipenem was approximately 80% in all samples of *Acinetobacter spp*. and *P. aeruginosa*, with polymyxin B exceeding 97%; however, high levels of resistance to other drugs were detected in these samples.[12] A new SENTRY microbiological investigation evaluated samples from 2006 to 2009 and revealed a temporal trend toward a reduction in the imipenem sensitivity in *Acinetobacter spp*. and *Klebsiella spp*. in all geographic regions. With the exception of *Acinetobacter spp*. and *Klebsiella spp*. from the Asia-Pacific and Latin America regions,[13] most isolates remained sensitive to polymyxins.

Mortality rates may be as high as 40%[14,15] and are related to, for example, a polymyxin B dose lower than 200mg per day, the presence of severe sepsis or septic shock, mechanical ventilation, renal failure, age and comorbidities.[16,17] Nephrotoxicity secondary to polymyxins has been reported since the earliest studies on the subject.[18] Certain studies have reported that up to 32% of patients using colistin develop acute kidney injury (AKI). Predisposing factors may include age, prior renal dysfunction, the use of other nephrotoxic drugs, a high dose of colistin and an elevated Acute Physiology and Chronic Health Evaluation II (APACHE II) score.[15,19] More recently, a lower incidence of renal failure associated with colistin therapy has been reported, and the therapy was well tolerated in critically ill patients with normal renal function.[20-23]

The purposes of this study are to describe a single center experience of the use of colistin to treat nosocomial infections caused by multidrug-resistant Gram-negative bacteria and to identify the factors associated with acute kidney injury and mortality.

METHODS

Study design and patients

This is a retrospective analysis of data prospectively collected from an ICU database. This longitudinal study aims to evaluate critically ill patients with nosocomial infection caused by multidrug-resistant Gram-negative bacteria who were treated with parenteral colistin at a general university hospital ICU. The adult ICU of the *Hospital Universitário da Universidade Estadual de Londrina* admits clinical and surgical patients, holds 17 beds and has an occupancy rate above 90% throughout the year.

This study has been approved by the local ethics committee (approval number: 284/05) and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The local ethics committee waived the need to obtain informed consent.

Patients were identified by the Nosocomial Infection Control Committee electronic database. All adult patients requiring treatment with intravenous colistin (colistimethate sodium) from January to December 2008 were considered eligible for the study. We performed a consecutive sampling that included all eligible patients during the study period. For patients admitted to the ICU more than once during the same period, the first admission in which colistin was administered was considered in the analysis. The exclusion criteria were age under 18 years, colistin use for less than 48 hours, use of colistin prior to ICU admission, use of polymyxin B and death occurring in less than 48 hours.

Data collection

For each patient, clinical data were extracted from the ICU database. The database included several variables, including age, gender, diagnosis and date of admission to the hospital and the ICU, first day of use and duration of treatment with colistin, date of and vital condition on discharge from the ICU and the hospital. We also analyzed data on the source of infection, dates of positive cultures and results of antimicrobial susceptibility testing. The database included APACHE II scores from the first 24 hours in the ICU[24] and the presence or absence of comorbidities. Side effects associated with the use of colistin (organ dysfunction; septic shock; invasive mechanical ventilation; dialysis; and the concomitant

use of vancomycin, amphotericin B, aminoglycoside, diuretics, and vasopressors) were recorded. To evaluate organ dysfunction, the Sequential Organ Failure Assessment (SOFA) score[25] was calculated throughout the ICU stay.

Variables and definitions

The primary outcome was defined as the 30-day mortality from all causes. The Centers for Disease Control (CDC) criteria[26] were adopted to diagnose hospital infection. The ACCP/SCCM (American College of Chest Physicians/Society of Critical Care Medicine) Consensus criteria[27] were adopted to diagnose sepsis. For each of the six organ systems evaluated using the SOFA score (neurological, cardiovascular, respiratory, renal, hematological and liver), organ failure was defined as a score greater than 2.[25]

The studied drug was colistimethate sodium (Promixin®, Opem Pharmaceuticals, 80mg = 1,000,000 IU). Patients who exhibited creatinine clearance (Crcl) greater than 80ml/minute received 5mg/kg/day of colistin; those who exhibited Crcl between 30 and 80ml/minute received 2.5mg/kg/day; and those who exhibited less than 30ml/minute received 1 to 1.5mg/kg/day. Creatinine clearance was estimated using the Cockcroft-Gault formula.[28] The dose was calculated based on the weight of the patient, and treatment duration was determined following recommendations of the local Nosocomial Infection Control Committee. An additional dose of 80 to 160mg was administered following hemodialysis. The treatment protocol followed local Nosocomial Infection Control Committee guidelines in all patients included in the present study. The possible combination therapies recommended by these guidelines included colistin associated with carbapenem and/or glycopeptides or linezolid. For microbiologically documented infections, antimicrobial susceptibility was tested using an automated method (MicroScan® - Dade Behring).

Use of a diuretic was defined as ≥40mg per day furosemide for at least 24 hours during colistin treatment. Use of vancomycin, amphotericin B or aminoglycoside was considered if the drug was employed over 48 hours during colistin treatment. The vasopressors considered in the analysis included dopamine, noradrenaline and adrenaline.

Acute kidney injury was identified according to the KDIGO definitions[29] as an increase in creatinine by 0.3mg/dL within 48 hours or as an increase in creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the prior seven days. For statistical analysis, patients were divided into those with and those without AKI during colistin use. Patients who received renal-replacement therapy prior to starting treatment with colistin were grouped into a third category (presence of kidney injury prior to colistin), which had no effect on the analysis of factors associated with AKI.

Statistical analysis

The descriptive statistical analysis used median and interquartiles or mean and standard deviation to describe the continuous variables, according to the data distribution. The Shapiro-Wilk test was used to assess the normal distribution of data. Percentages were used to describe the categorical variables. Data are presented using tables. The Chi-square test was used to compare the categorical variables, and the Mann-Whitney test was used to compare the continuous variables. The dependent variables tested in the univariate analysis for death and AKI included the following: sex; age; comorbidities; length of stay in the hospital and in the ICU before colistin prescription; mechanical ventilation; concomitant use of other antibiotics, diuretics and vasopressors; micro-organism; and site of infection. For the logistic-regression model, the variables for which the p values were ≤0.2 in the univariate analysis were included one by one in a forward stepwise method. The results were described as frequency, odds ratio (OR) and 95% confidence interval (CI) or as median and interquartile ranges. Patient survival is described using a Cox proportional hazards regression model that considers the confounding factors. A stepwise forward method was applied by entering the relevant variables sequentially and after checking them, removing the non-significant variables; these results are described as a hazard ratio (HR) and 95%CI. A p value of 0.05 was considered significant. The area under the receiver operating characteristic (ROC) curve was used to assess the accuracy of the findings and compare the performance of APACHE II and SOFA in discriminating survivors from non-survivors. Data were analyzed using Medcalc 12 (MedCalc Software, Belgium).

RESULTS

Patients, sources of infection and microorganisms

During the study period, colistin was used to treat an infection in 109 (13.8%) of the 789 patients admitted to the ICU. Baseline patient characteristics are summarized in table 1. These patients had a median age of 66 (48-75) years and were mostly male (66.1%). The median APACHE II score was 25 (20-32) upon ICU admission. The median SOFA score at ICU admission was 9 (6-12), and there was no significant difference compared to the SOFA score at the beginning of colistin treatment (8 [6-11]; p=0.142). The 30-day mortality observed in these patients was 71.6%. In 79 (72.5%) patients, colistin was started empirically before obtaining results from cultures, according to Nosocomial Infection Control Committee guidelines. Colistin treatment was begun an average of 10 (6-14.2) days after admission to the ICU. The median serum creatinine was 1.25 (0.93-2.11) mg/dL upon admission to the ICU and 1.49 (0.90-2.29) mg/dL at the start of treatment. Twenty-nine (26.6%) patients were receiving renal-replacement therapy prior to starting colistin treatment. Twenty-one (19.2%) patients developed AKI, 11 of whom required dialysis after starting colistin and 9 of whom needed diuretic therapy. Invasive mechanical ventilation was administered to 105 (96.3%) patients, with a mean duration of 12.4±8.8 days. Vasopressors were used in 73 (66.9%) patients for a mean of 3.2±4.6 days.

VAP was the most frequent infection site (76/109, 69.7%), followed by bloodstream infection (BSI; 15/109, 13.7%), surgical-site infection (8/109, 7.3%), urinary-tract infection (7/109, 6.4%), peritonitis (2/109, 1.9%), and skin and soft-tissue infections (1/109, 0.9%). Infections were microbiologically confirmed in 102 patients, and 7 VAP cases had negative cultures. Among patients with positive cultures, *A. baumannii* was isolated in 52 cases (50.9%) and was the causative microorganism in 48 patients with VAP and in 3 patients with BSI. *P. aeruginosa* was isolated in 23 (22.5%) patients and was the etiologic agent in 10 patients with VAP and in 4 patients with BSI. Eight cases (7.8%) were positive for the both microorganisms (*A. baumannii and P. aeruginosa*), 7 from tracheal secretions and 1 from a blood culture. Other microorganisms isolated less frequently included *Candida sp.* (3.9%), *Escherichia coli* (2.9%), *Enterococcus faecium* (1.9%), *Stenotrophomonas maltophilia* (1.9%), *Enterobacter cloacae* (1.9%), *Staphylococcus aureus* (0.9%), *Delftia acidovorans* (0.9%), *Staphylococcus haemolyticus* (0.9%), *Klebsiella pnuemoniae* (0.9%), *Burkholderia cepaia* (0.9%), and *Providencia stuarti* (0.9%). All *A. baumannii* and *P. aeruginosa* isolates were resistant to carbapenem, aminoglycosides, quinolones, ampicillin-sulbactam and piperacillin-tazobactam.

Table 1 - General characteristics of 109 patients treated with colistin

	Results
Men	72 (66.1)
Age (years)	66 (48-75)
Length of stay in the ICU (days)	21 (12.75-31)
Length of stay in the hospital (days)	32 (20-53.5)
APACHE II	25 (20-32)
SOFA at ICU admission	9 (6-12)
SOFA at the beginning of colistin treatment	8 (6-11)
Associated use of vancomycin	35 (32.11)
Associated use of amphotericin B	5 (4.59)
Associated use of aminoglycoside	5 (4.59)
Associated use of diuretics	38 (34.86)
Associated use of vasopressors	73 (66.97)
Mechanical ventilation	105 (96.33)
Treatment duration (days)	10 (5-15)
Empirical beginning of treatment	79 (72.48)
Concordance with positive cultures (n=79)	58 (73.42)
Days since the beginning of treatment	10 (6-14.25)
Creatinine at ICU admission (mg/dl)	1.25 (0.93-2.11)
Creatinine at the beginning of treatment (mg/dl)	1.49 (0.90-2.29)
Acute kidney injury	
Patients on hemodialysis before treatment	29 (26.61)
Patients not on hemodialysis before treatment (n=80)	
Absence of acute kidney injury	59 (73.75)
Presence of acute kidney injury	21 (26.25)
All-cause hospital mortality	91 (83.49)
All-cause 30-day mortality	78 (71.56)

ICU - intensive care unit; APACHE II - Acute Physiology and Chronic Health Evaluation II; SOFA - Sequential Organ Failure Assessment. Results expressed as number (%) or median (25%-75%).

Factors associated with acute kidney injury

Twenty-nine patients presented kidney injury and received dialysis prior to colistin treatment; these patients were therefore not included in the analysis of risk factors for the development of AKI. Among these patients on dialysis before treatment with colistin, we observed that 7/29 (24.1%) were able to recover kidney function and eliminate the need for dialysis even during colistin treatment.

Twenty-one out of 80 patients (26.2%) examined fulfilled acute kidney injury criteria while on colistin during the study period. There was no difference between the groups (with or without AKI) for any of the variables evaluated, with the exception of the SOFA score at the beginning of treatment (OR 1.46; 95%CI 1.2-1.79; p<0.001), vasopressor drug use (OR 4.72; 95%CI 1.25-17.8; p=0.010) and serum creatinine at the beginning of treatment (OR 1.94; 95%CI 1.12-3.38; p=0.010). In the logistic-regression model, the variable independently associated with the presence of AKI was the SOFA score at the beginning of colistin treatment (OR 1.46; 95%CI 1.20-1.79; p<0.001; Table 2).

Factors associated with death

The univariate analysis revealed that age (OR 1.02; 95%CI 1.00-1.04; p=0.028), SOFA score on the first day of colistin treatment (OR 1.30; 95%CI 1.12-1.51; p=0.001) and the use of vasopressors (OR 11.17; 95%CI 4.24-29.40; p<0.001) were associated with death. In the logistic-regression model, age (OR 1.03; 95%CI 1.00-1.05; p=0.027) and the use of vasopressors (OR 12.48; 95%CI 4.49-34.70; p<0.001) were independently associated with death (Table 3).

ROC curves were used to analyze the APACHE II and SOFA data at ICU admission and the SOFA score on the first day of colistin treatment. The areas under the curve were 0.545 (95%CI 0.447-0.641; p=0.449) for APACHE II, 0.530 (95%CI 0.432-0.626; p=0.618) for SOFA at ICU admission and 0.724 (95%CI 0.631-0.806; p<0.001) for SOFA on the first day of colistin treatment. The cut-off point for APACHE II was 30 (34.6% sensitivity and 83.8% specificity); the cut-off for the SOFA score was 8 (56.4% sensitivity and 54.8% specificity) at ICU admission and 9 (47.4% sensitivity and 90.3% specificity) on the first day of colistin treatment.

There was no difference in survival probability for the groups of patients divided according to the presence of AKI (HR=1.019; 95%CI 0.646-1.608; p=0.933); however, the use of vasopressors was a determining factor of the 30-day survival probability (HR=4.093; 95% CI 2.286-7.326; p<0.001) (Figure 1).

DISCUSSION

Treatment with colistin was common among the study sample, as 13.8% of ICU patients acquired nosocomial infections caused by multidrug-resistant organisms during the study period. These infections were microbiologically documented, and carbapenem-resistant *A. baumannii* and *P. aeruginosa* were present in most patients. AKI was frequent in these patients, and in several cases, this condition could not be associated with colistin because it occurred even before colistin was initiated. The SOFA score on the first day of colistin treatment was associated

Table 2 - Univariate and multivariate analysis of factors associated with acute kidney injury in 80 patients treated with colistin

	Univariate analysis			Logistic regression		
	Odds ratio	95%CI	p value	Odds ratio	95%CI	p value
Men	1.654	0.578-4.732	0.352			
Age (years)	1.003	0.977-1.029	0.843			
Length of stay in the ICU (days)	0.956	0.911-1.002	0.029			
Length of stay in the hospital (days)	0.975	0.951-0.999	0.018			
APACHE II	1.017	0.945-1.094	0.657			
SOFA at ICU admission	1.082	0.930-1.258	0.304			
SOFA at the beginning of colistin treatment	1.467	1.202-1.789	<0.001	1.467	1.202-1.789	<0.001
Associated use of vancomycin	1.529	0.559-4.181	0.409			
Associated use of amphotericin B	0.933	0.092-9.498	0.953			
Associated use of aminoglycoside	1.425	0122-16.579	0.781			
Associated use of diuretics	0.425	0.137-1.315	0.123			
Associated use of vasopressors	4.727	1.255-17.802	0.010			
Mechanical ventilation	3.486	0.180-67.546	0.408			
Treatment duration (days)	0.940	0.867-1.020	0.117			
Creatinine at ICU admission (mg/dl)	1.071	0.630-1.823	0.802			
Creatinine at the beginning of treatment (mg/dl)	1.949	1.124-3.380	0.010			

95%CI - 95% confidence interval; ICU - Intensive Care Unit; APACHE II - Acute Physiology and Chronic Health Evaluation II; SOFA - Sequential Organ Failure Assessment.

Table 3 - Univariate and multivariate analysis of factors associated with 30-day mortality in 109 patients treated with colistin

	Univariate analysis			Logistic regression		
	Odds ratio	**95%CI**	**p value**	**Odds ratio**	**95%CI**	**p value**
Men	0.909	0.379-2.177	0.831			
Age (years)	1.023	1.002-1.044	0.028	1.027	1.003-1.052	0.027
APACHE II	1.021	0.970-1.074	0.426			
SOFA at ICU admission	1.040	0.929-1.163	0.495			
SOFA at the beginning of colistin treatment	1.303	1.121-1.516	0.001			
Associated use of vancomycin	1.522	0.601-3.857	0.368			
Associated use of amphotericin B	1.622	0.174-15.111	0.658			
Associated use of aminoglycoside	1.622	0.174-15.111	0.658			
Associated use of diuretics	0.963	0.403-2.300	0.932			
Associated use of vasopressors	11.175	4.247-29.402	<0.001	12.485	4.492-34.703	<0.001
Mechanical ventilation	0.833	0.083-8.332	0.875			
Empirical beginning of treatment	2.105	0.861-5.149	0.103			
Concordance with positive cultures (n=79)	0.437	0.113-1.689	0.230			
Days for beginning of treatment	1.001	0.940-1.065	0.982			
Creatinine at ICU admission (mg/dl)	1.010	0.744-1.370	0.950			
Creatinine at the beginning of treatment (mg/dl)	1.187	0.812-1.734	0.365			
Acute kidney injury	1.530	0.905-2.586	0.102			

95%CI - 95% confidence interval; ICU - Intensive Care Unit; APACHE II - Acute Physiology and Chronic Health Evaluation II; SOFA - Sequential Organ Failure Assessment.

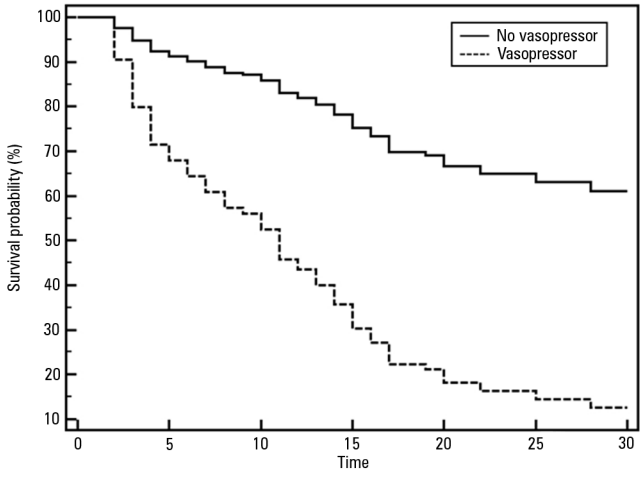

Figure 1 - Cox proportional hazards regression model evaluating the survival probability of patients treated with colistin, according to the use of vasopressors. Time = days; Hazard ratio = 4.093 (95% confidence interval 2.286-7.326); p<0.001.

with a worsening of renal function. AKI was not associated with higher mortality. Age and the need for vasopressors were factors associated with death.

An increase in the incidence of infections caused by *A. baumannii* and *P. aeruginosa* has been reported in critically ill patients. Malignant disease, hemodialysis, and ICU stay are known risk factors for infection caused by imipenem-resistant *A. baumannii*.[9] Prior use of β-lactam antibiotics and fluoroquinolones, neurological disease, urinary-tract infection, kidney disease and admission to the ICU are associated with infections caused by metallo-beta-lactamase-producing strains of *P. aeruginosa*.[10]

The nephrotoxicity of polymyxins has been described since the earliest studies on these compounds and was reported to be associated with higher doses of the drug.[18] Other factors may also be involved; in 1970, Koch-Weser et al. analyzed 317 therapy courses and found that 20.2% were associated with renal toxicity.[19] In addition to the colistin dose, the following factors were also associated with AKI: previous renal dysfunction, simultaneous use of cephalothin, duration of treatment and age. There was no adjustment for the severity of illness; however, although AKI was more frequent among patients using vasopressors, that association was not statistically significant.[19]

Levin et al. reported that 32% of patients presented creatinine levels above 1.5 mg/dL, with an average colistin dose of 152.8mg.[15] Recently, another study involving approximately 65% of an ICU patient population reported that 14% of the sample developed AKI. The treatment dose was 5mg/kg for patients with normal renal function and was adjusted as the creatinine clearance (Crcl) declined. The APACHE-II score, age, length of stay and comorbidities were not associated with AKI.[30]

In our patients, we observed an increase in creatinine levels even before the use of colistin, and AKI was associated with a higher SOFA score at the beginning of treatment. Therefore, we were unable to attribute the presence of AKI exclusively to the use of colistin but rather as one of the diagnostic factors for multiple organ failure due to the severity of illness, along with other factors, such as concomitantly administered potential nephrotoxic agents. However, we also observed a group of patients who recovered renal function during colistin use, most likely due to control of the infection, recovery from shock and clinical improvement. Recent data from published reports suggest that colistin is a safe therapeutic intervention to treat infections caused by multidrug-resistant Gram-negative bacteria.[21-23]

The mortality rate observed in our study was high, and data on the length of ICU stay indicates an early progression to death. None of the scores evaluated using ROC curves performed well, with areas under the curve falling below 0.8. Age and the need for vasopressors were risk factors associated with death. Considering the current recommendation for using higher doses to treat these severe infections, we speculate that our results revealing elevated mortality rates could be due to the lower daily dose delivered to our patients.

In one of the first reports of the reintroduction of colistin into clinical practice, Levin et al. reported the use of 2.5 to 5mg/kg to treat infections caused by *A. baumannii* and *P. aeruginosa* in 59 patients; they described a 42% mortality rate.[15] The mortality in these patients may be related to several risk factors,[17] including low doses of polymyxin B.[16]

There are a few limitations in our study that must be considered. The retrospective design of the study, despite analyzing data from a prospectively collected database, presents an inherent weakness. The sample of 109 patients may have resulted in insufficient power to identify other factors associated with the evaluated outcomes. Our study lacks data on the sensitivity to colistin, and this factor may have contributed to ineffective treatments and subsequently to the high mortality rate observed. The recommended dose for treating these infections at the time of data collection may be considered low. Our study also lacks data on other potentially nephrotoxic interventions; therefore, we were unable to attribute AKI exclusively to colistin use. A recent population study of colistin pharmacokinetics suggests using higher doses than those administered to our patients.[31] The KDIGO definitions for AKI did not include data on the urine volume, as our database does not include this information. Therefore, AKI may have been under diagnosed in our sample. Nevertheless, relevant clinical information emerged from the study. In this group of critically ill patients, AKI was not associated with increased mortality. Despite the view of AKI as a major adverse effect of colistin, kidney function improvements were observed in patients with a good clinical response to colistin treatment.

CONCLUSION

In conclusion, our study describes the experience of a single center with the use of colistin to treat nosocomial infections. We observed a high frequency of patients with infections caused by multidrug-resistant Gram-negative bacteria, and these patients presented high mortality rates; however, we encourage administering colistin to these patients, as it is one of the last therapeutic options remaining to treat these infections. AKI was associated with a higher SOFA score at the beginning of colistin use. In a small group of patients, we were able to observe improvements in the kidney function during colistin treatment. Age and vasopressor use were associated with a higher mortality rate.

RESUMO

Objetivo: Descrever a experiência de um único centro com o uso de colistina para tratar infecções hospitalares causadas por bactérias *Gram-negativas* resistentes a múltiplos fármacos e identificar fatores associados com lesão renal aguda e mortalidade.

Métodos: Estudo longitudinal retrospectivo que avaliou pacientes gravemente enfermos, com infecções causadas por bactérias *Gram-negativas* resistentes a múltiplos fármacos. Foram considerados elegíveis para este estudo, durante o período compreendido entre janeiro e dezembro de 2008, todos os pacientes adultos com necessidade de tratamento com colistina endovenosa (colistimetato de sódio). As informações coletadas incluem dados demográficos, diagnóstico, duração do tratamento, presença de lesão renal aguda e mortalidade em 30 dias.

Resultados: A colistina foi utilizada para tratar uma infecção em 109 de 789 pacientes (13,8%) admitidos à unidade de terapia intensiva. A mortalidade em 30 dias observada nestes pacientes foi de 71,6%. Vinte e nove pacientes (26,6%) tinham lesão renal prévia ao tratamento com colistina, sendo que seis deles conseguiram recuperar a função renal, mesmo

durante o tratamento com colistina. Vinte e um pacientes (19,2%) desenvolveram lesão renal aguda durante o tratamento com colistina, sendo que 11 destes pacientes necessitaram ser submetidos à diálise. A variável independentemente associada com a presença de lesão renal aguda foi a pontuação segundo o sistema *Sequential Organ Failure Assessment* no início do tratamento com colistina (OR=1,46; IC95%=1,20-1,79; p<0,001). Idade (OR=1,03; IC95%=1,00-1,05; p=0,02) e uso de vasopressores (OR=12,48; IC95%=4,49-34,70; p<0,001) foram fatores associados a óbito, segundo um modelo de regressão logística.

Conclusões: Disfunção de órgão quando do início do tratamento com colistina associou-se com lesão renal aguda. Em um pequeno grupo de pacientes, pudemos observar uma melhora da função renal durante o tratamento com colistina. Idade e uso de vasopressores associaram-se a óbito.

Descritores: Colistina/uso terapêutico; Cuidados intensivos; Infecção hospitalar/quimioterapia; *Acinetobacter baumannii*; *Pseudomonas aeruginosa*; Lesão renal aguda; Morte

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