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Original Article

Clinical outcome of pediatric patients using polymyxin B

Desfechos clínicos de pacientes pediátricos em uso de Polimixina B

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ABSTRACT

Objective: to evaluate the clinical effectiveness and safety of polymyxin B in the treatment of infections caused by bacteria resistant to multiple drugs. **Methods:** a retrospective cohort was carried out, evaluating the medical records of diagnosed patients with infections caused by bacteria resistant to multiple drugs and treated with polymyxin B (from January 2018 to December 2020, in intensive care units of a pediatric hospital in Salvador – Ba. Safety was assessed using the nephrotoxicity criteria established by Kidney Disease: Improving Global Outcomes. **Results:** a total of 39 patients used polymyxin B for infections caused by bacteria resistant to multiple drugs, with treatment success being achieved in 13 (33.3%) patients with clinical and/or microbiological cure, while the Mortality was observed in 26 (66.6%) patients, of which 19 (73%) were described in a medical report as death related to infection and 7 (27%) were associated with complications from comorbidities. The occurrence of kidney injury was reported in 21 patients, of which 6 were discarded to do renal damage before the use of polymyxin B, 15 (38.4%) with a rate of nephrotoxicity classified as stages 1, 2, and 3, according to the Kidney Disease: Improving Global Outcomes criteria. **Conclusion:** approximately one third of patients were clinically and microbiologically cured. It is necessary to carefully evaluate treatment with polymyxin B, prioritizing multidrug-resistant infections, rational use and attention to monitoring renal function.

Keywords: multidrug resistance; polymyxin B; drug toxicity; child; Bacterial resistance.

RESUMO

Objetivo: avaliar a efetividade clínica de polimixina B no tratamento de infecções por bactérias resistentes a múltiplas drogas e a segurança através dos critérios de nefrotoxicidade estabelecidos por *Kidney Disease: Improving Global Outcomes*. **Metódos:** foi realizada uma coorte retrospectiva, com avaliação dos prontuários de pacientes que utilizaram o medicamento para tratar infecções por bactérias resistentes a múltiplas drogas (no período de janeiro de 2018 a dezembro de 2020, em unidades de terapia intensiva de um hospital pediátrico de Salvador – Ba. **Resultados:** um total de 39 pacientes usaram polimixina B para infecções por bactérias resistentes a múltiplas drogas, sendo que o sucesso do tratamento foi obtido em 13 (33,3%) pacientes com a cura clínica e/ou microbiológica, enquanto a mortalidade foi observada em 26 (66,6%) pacientes, dentre esses, 19 (73%) foram descritos em relatório médico como óbito relacionado à infecção e 7 (27%) associados às complicações das comorbidades. A ocorrência de lesão renal foi relatada em 21 pacientes, dos quais 6 foram descartados por apresentarem lesão renal prévia ao uso da polimixina B, 15 (38,4%) com taxa de nefrotoxidade classificados em estágios 1, 2 e 3, segundo os critérios de *Kidney Disease: Improving Global Outcomes*. **Conclusão:** aproximadamente um terço dos pacientes tiveram cura clínica e microbiológica. Faz-se necessária a avaliação cautelosa do tratamento com polimixina B, priorizando as infecções multirresistentes, o uso racional e atenção para monitoramento da função renal.

Palavras-chave: Resistência a Múltiplas Drogas; Polimixina B; Toxicidade de Medicamentos; Criança; Resistência Bacteriana.

Introduction

Polymyxins (polymyxin B and polymyxin E [colistin]) are antibiotics with main activity against gram-negative bacilli, discovered more than 60 years ago. Due to reports of renal and neurological toxicity associated with their use, and with the development of antimicrobials with lower toxicity potential, polymyxins ceased to be used routinely in the mid-1970s. However, due to the emergence of multidrug-resistant microorganisms, the use of polymyxins was resumed as one of the few therapeutic options in the late 1980s.[1]

Antimicrobial resistance has become a threat to public health. The spread of carbapenem resistance among Enterobacteriaceae has emerged in the last 15 to 20 years, due to the production of carbapenemase enzymes by these bacteria.[2] Multidrug-resistant gram-negative microorganisms, known as "superbugs", such as Acinetobacter baumannii, Pseudomonas aeruginosa, and Klebsiella pneumoniae, often remain susceptible to polymyxins, which are used as one of the last therapeutic options in combination with other antimicrobials.[3]

However, recent studies have reported polymyxin resistance through a plasmid-mediated mechanism.[2] Multidrug resistance to antibiotics, in addition to increasing morbidity and mortality, also increases health care costs. Factors such as excessive use of antimicrobials and the natural development of microbial resistance contribute to the occurrence and spread of this problem.[4]

Reports of polymyxin B use in the pediatric population are scarce, and pharmacokinetic data are limited, mostly old, and carried out when polymyxins were more widely used, around the 1980s. A retrospective study conducted in a pediatric hospital showed increased use of polymyxin B in critically ill patients for the treatment of Multidrug-Resistant (MDR) infections, due to the high rates of carbapenem-resistant gram-negative bacteria.[5]

Polymyxins have a high potential to cause nephrotoxicity, through a mechanism related to drug accumulation in the epithelial cells of the proximal renal tubule and consequent increase in membrane permeability, leading to acute tubular necrosis, which usually limits treatment. Concomitant exposure to other nephrotoxic drugs may favor the development of Acute Kidney Injury (AKI), especially in severely ill children. Most pediatric studies report rates of 3 to 10% renal toxicity, however, incidences greater than 20% have been described.[6]

Nephrotoxicity is defined as the occurrence of AKI induced by polymyxin B. AKI can be classified according to the criteria of "Kidney Disease: Improving Global Outcomes" (KDIGO), with stage 1 defined as serum creatinine ≥0.3 mg/dL in 48 hours or 1.5 to 1.9 times baseline creatinine in 7 days; stage 2 as serum creatinine 2 to 3 times baseline; and stage 3 as serum creatinine >3 times baseline or ≥4 mg/dL, or if renal replacement therapy is required.[7]

Considering the growing use of polymyxin B due to the progressive emergence of multidrug-resistant microorganisms, with scarce therapeutic options beyond this class of antimicrobials, in addition to recent reports of resistance to polymyxins, coupled with the insufficient amount of literature data related to nephrotoxicity and its incidence in the pediatric population, it is necessary to conduct a study to evaluate clinical outcomes and the safety of polymyxin B use for the treatment of multidrug-resistant bacterial infections, using a standardized classification of acute kidney injury.

The present study aims to evaluate the clinical outcomes of pediatric and neonatal patients after the use of polymyxin B for the treatment of multidrug-resistant bacterial infections.

Materials and methods

This is a retrospective cohort study conducted in a pediatric hospital with 220 beds and care accredited by the Unified Health System (SUS). The hospital has a Neonatal Intensive Care Unit (NICU) and two pediatric ICUs, with a total of thirty beds.

The inclusion criteria were: being hospitalized in the pediatric and neonatal ICUs and having an antibiogram with a positive result for MDR. The following exclusion criteria were considered: need

for dialysis within 48 hours prior to the introduction of polymyxin B and/or previous renal dysfunction, death occurring within less than 48 hours after the start of polymyxin B treatment, and use of polymyxin B for a period shorter than 48 hours.

For data collection, patients were selected through the medication consumption report available in the hospital's virtual system, containing all patients who used polymyxin B from January 2018 to December 2020. From the report generated by the pharmacy sector, patient records were retrieved for review and data collection in a form created in Excel®. The following data were collected: sex, age, weight, height, main diagnosis, medical history and length of hospitalization, dose and duration of polymyxin B use, record of antibiotic and nephrotoxic drug use, serum creatinine dosage, infection site, etiological agent, and antibiotic susceptibility profile through antibiogram. All these data were collected from the electronic medical records, which included not only demographic characteristics but also results of various laboratory tests, microbiological cultures, and antibiograms.

Data analyses were performed in Excel®, and results were expressed as mean or median with their respective measures of dispersion for continuous variables, and as absolute and relative frequencies for categorical variables.

This study was approved by the Research Ethics Committee of Maternidade Climério de Oliveira - UFBA (CEP Opinion No. 4.416.739).

Results

Among 199 patients who received polymyxin B in the pediatric and neonatal ICU, a total of 41 had a resistance profile identified through antibiogram as multidrug-resistant (MDR) bacteria. Two of these were excluded due to polymyxin B use for less than 48 hours because of death, leaving 39 patients for data analysis. The general characteristics of the studied sample are described in Table 01. The mean daily dose and duration of polymyxin B therapy were 37,307 IU/kg/day divided into two doses per day, and 12 days, respectively.

Table 01. Characteristics of patients undergoing polymyxin B therapy.

Characteristics	Patients (N = 39)
Sex	N %
Female	18 (46.2%)
Maler	21 (53.8%)
Hospital Unit	N %
Neonatal ICU	13 (33.3%)
Pediatric ICU A	9 (23.1%)
Pediatric ICU B	17 (43.6%)
Age Group	N %
Neonatal (0 - 28 dias)	7 (17.9%)
Infant (29 dias - 2 anos)	26 (66.7%)
Preschool (2 - 4 anos)	2 (5.1%)
School-age (5 - 10 anos)	2 (5.1%)
Adolescent (11 - 19 anos)	2 (5.1%)
Underlying Disease	N %
Congenital heart disease	20 (51.3%)
Oncological disease	7 (17.9%)
Intestinal obstruction	6 (15.4%)
Encephalopathy	4 (10.3%)
Pneumonia with pleural effusion	1 (2.6%)
Peritonitis	1 (2.6%)
Length of ICU stay (days)	45 ± 30 (X ± SD)

X = mean; SD = standard deviation
Source: Prepared by the authors

Regarding clinical outcomes, treatment success was observed in 13 (33.3%) patients who achieved cure, while mortality was reported in 26 (66.6%) patients. Among these, 19 (73%) were described in medical records as death related to infection, and 7 (27%) were associated with other comorbidities and complications (Table 02).

Table 02. Clinical outcomes of patients treated with polymyxin B.

Clinical Outcome	Patients
	(N = 39%)
Cure	13 (33.3%)
Death	26 (66.6%)
	N= 26 (%)
Death related to infection	19 (73%)
Death related to other comorbidities	7 (27%)

Source: Prepared by the authors

The most common site of pathogen isolation was the bloodstream (18 patients; 46.1%), followed by tracheal secretion (10 patients; 25.6%). Other sites included catheter tip (3 patients; 7.7%), pleural fluid (3 patients; 7.7%), and others (5 patients; 12.8%). The most frequently isolated bacteria were Klebsiella pneumoniae (15 patients; 38.5%), Acinetobacter baumannii (10 patients; 25.3%), and Pseudomonas aeruginosa (8 patients; 20.5%), in addition to others with lower incidence, which are described in Table 03. Klebsiella pneumoniae was the bacterium most associated with mortality (11 deaths, 57.9%).

Nephrotoxicity was assessed through daily measurement of serum creatinine before, during, and after the use of polymyxin B. According to KDIGO criteria, the occurrence of acute kidney injury (AKI) was reported in 21 (53.8%) patients, of whom 6 (28.5%) were excluded from nephrotoxicity evaluation due to preexisting AKI before polymyxin B use, leaving 15 (38.4%). The excluded patients had the following underlying conditions: hepatoblastoma 1 (16.6%), congenital heart disease 3 (50%), necrotizing enterocolitis 1 (16.6%), and endocarditis 1 (16.6%).

The classification according to KDIGO is described in Table 04. Eight (53.3%) patients were classified as stage 1, where serum creatinine is greater than or equal to 0.3 mg/dL in 48 hours or 1.5 to 1.9 times baseline creatinine within 7 days; four (26.6%) as stage 2, where serum creatinine is greater than 2 to 3 times baseline; and three (20%) as stage 3, where serum creatinine is greater than 3 times baseline or greater than or equal to 4 mg/dL, or if renal replacement therapy is required.

Table 03. Site of pathogen isolation and etiological agent.

Organisms	n(%)	Total blood n(%)	Tracheal secretion n(%)	Catheter tip n(%)	Pleural fluid n(%)	Others n(%)
Klebsiella pneumonie	15 (38.5%)	13 (33.3%)	2 (5.1%)	0	0	0
Acinectobacter baumannii	10 (25.3%)	3 (7.7%)	2 (5.1%)	0	2 (5.1%)	3 (7.7%)
Pseudomonas aeruginosa	8 (20.5%)	0	5 (12.8%)	1 (2.6%)	1 (2.6%)	1 (2.6%)
Pseudomonas fluorescens	2 (5.1%)	0	1 (2.6%)	1 (2.6%)	0	0
Enterobacter cloacae	2 (5.1%)	1 (2.6%)	0	1 (2.6%)	0	0
Serratia sp. / Citrobacter feundii	1 (2.6%)	0	0	0	0	1 (2.6%)
Enterobacter aerogenes / Aeromonas hydrophila	1 (2.6%)	1 (2.6%)	0	0	0	0
Total	39 (100%)	18(46.1%)	10 (25.6%)	3 (7.7%)	3 (7.7%)	5(12.8%)

Source: Prepared by the authors

Table 04. Classification of nephrotoxicity according to Kidney Disease: Improving Global Outcomes (KDIGO) criteria.

		N= 39 (%)
Nephrotoxicity		15 (38,4%)
		N= 15 (%)
Stage 1		8 (53,3%)
Stage 2		4 (26,6%)
Stage 3		3 (20%)
Patients N= 15	**Mean Baseline Creatinine (mg/dL)**	**Mean Outcome Creatinine (mg/dL)**
Patient 01	0,36	0,8
Patient 02	0,26	0,71
Patient 03	0,35	2,04
Patient 04	0,24	0,55
Patient 05	0,22	0,59
Patient 06	0,26	0,61
Patient 07	0,28	0,77
Patient 08	0,43	0,9
Patient 09	0,31	1,25
Patient 10	0,12	0,36
Patient 11	0,16	0,49
Patient 12	0,16	0,31
Patient 13	0,22	0,72
Patient 14	0,57	0,86
Patient 15	0,58	1,1

Source: Prepared by the authors

Two (5.1%) patients required renal replacement therapy after treatment through peritoneal dialysis (PD). Among the patients who developed some degree of kidney injury, dose adjustment for renal dysfunction was performed in 3 (20%) patients, with a reduction of up to 50% of the dose.

Among the patients who received combination antimicrobial therapy, approximately 37 (94.8%, n=39) received between 2 and 4 antimicrobials per day and 2 (5.1%, n=39) received 5 or more. The most common combinations were: Polymyxin B + Amikacin (18%), Polymyxin B + Meropenem + Vancomycin (15.4%, n=39), and Polymyxin B + Amikacin + Vancomycin (12.8%, n=39), in addition to the concomitant use of other nephrotoxic medications, which significantly increase the risk of nephrotoxicity.

Discussion

In the present study, the mean daily dose and duration of polymyxin B therapy were 37,307 IU/kg/day divided into two doses per day, and 12 days, respectively. The international consensus guidelines for the optimal use of polymyxins are based only on studies conducted in adults, due to the scarcity of studies on this subject in pediatrics and neonatology, therefore its use is considered "off label" in children and neonates. The consensus recommendations are for a loading dose of 20,000 to 25,000 IU/kg, infused over one hour, and a maintenance dose of 12,500 to 15,000 IU/kg every 12 hours for severe infections with normal renal function. However, the guidelines report doses exceeding 30,000 IU/kg and highlight the need for studies to define safety, as well as the clinical and microbiological impact of this practice.[8]

Regarding clinical outcomes, a considerable mortality rate was observed as directly related to infection. A retrospective cohort study analyzed the use of polymyxin B for the treatment of multidrug-resistant (MDR) gram-negative infections in pediatric patients admitted to the ICU of a university hospital. The mortality rate in patients treated

with polymyxin B was 42.9%, of which 75% were under one year of age. In the present study, a higher rate (73%) was observed with death directly related to infection.[5]

It is difficult to determine whether microbial resistance is the cause of death in ICU patients with severe conditions and multiple associated comorbidities, in addition to the possible worsening of the clinical condition and/or adverse reactions, since these patients are polymedicated and mostly undergo prolonged antibiotic treatment.

The bacterium most associated with mortality (11 deaths, 57.9%) was Klebsiella pneumoniae, similar to the prospective cohort study by Mattos et al. (2019), which evaluated the clinical outcome of polymyxin B therapy in infections caused by multidrug-resistant bacteria in adult patients from a university hospital in Brazil. They observed that Klebsiella pneumoniae, a carbapenemase producer, was the most prevalent etiological agent in infections and the most associated with mortality (18 deaths, 22.2%). The study reported a mortality rate of 32.8%, treatment success in 25.1%, and nephrotoxicity in 40.5%.[9]

In a multicenter retrospective case-control study, risk factors for colonization or infection by carbapenem-resistant Enterobacteriaceae were evaluated over nearly 5 years in three pediatric hospitals in the United States. The authors identified that exposure to broad-spectrum antibiotics, in addition to mechanical ventilation and recent surgery, were significant risk factors for colonization or infection by multidrug-resistant bacteria. This reinforces the importance of antimicrobial stewardship interventions aimed at limiting unnecessary use of these antibiotics, especially in patients considered at high risk.[10]

The combination of antimicrobials was widely used during the treatment of MDR infections. The literature presents controversies regarding combination therapy versus polymyxin B monotherapy. Given the emergence and spread of multidrug-resistant bacteria, combination therapy becomes an important strategy. The risk-benefit must be carefully assessed, with the main target organisms resistant to carbapenems being Enterobacteriaceae, A. baumannii, and P. aeruginosa.[8]

Regarding nephrotoxicity, although most patients were classified as stage 1 AKI, the frequency was high (38.4%). It is difficult to attribute it as an adverse reaction exclusively of polymyxin B, since most ICU patients receive a therapeutic arsenal that can contribute as a risk factor for kidney injury. Nephrotoxic drugs, as pointed out by Tjon and Teon (2020), most commonly observed in concomitant or prior use to polymyxin B therapy, were amikacin, amphotericin B, vancomycin, furosemide, omeprazole, and phenytoin. The international consensus recommendation for optimal use of polymyxin B is to avoid concomitant use with nephrotoxic drugs whenever possible, as this is a risk factor for AKI.[11,8]

The greater the intensity of exposure to polymyxin B, in terms of dose, the higher the risk of causing AKI. The incidence of nephrotoxicity related to polymyxin B use varies widely in the literature, ranging from 0% to over 60%, which is due to the heterogeneity of the studied populations, the divergence in nephrotoxicity definitions, and the wide range of doses administered in clinical practice. In the previously cited study, with a high mortality rate in pediatric patients, nephrotoxicity was also observed in 21.4% of patients.[8,5]

Another study evaluated the prevalence of acute kidney injury according to KDIGO criteria and the determining factors associated with AKI in pediatric patients in an intensive care unit. Some variables were associated with a higher risk of developing AKI, such as sepsis, use of vasoactive drugs, and ventilatory support. Similarly, a retrospective analysis study that identified risk factors for the development of AKI in patients in a Pediatric Intensive Care Unit reported an incidence of acute kidney injury of 64% in 434 evaluated patients, with risk factors including mechanical ventilation, low urine output, and positive fluid balance, in addition to the use of drugs such as vasoactive agents, diuretics, and amphotericin. Considering that the population of the present study comes from the ICU and is exposed to the mentioned variables, they are at higher risk of developing AKI regardless of polymyxin B use.[12,13]

For patients who presented some type of kidney injury, dose adjustment was performed with up to

50% reduction. According to the international consensus guidelines, dose adjustment of polymyxin B is not required in patients with renal impairment, since studies demonstrate that polymyxin B is not completely eliminated by the kidneys and its clearance does not depend on creatinine clearance. Unnecessary dose adjustments may increase the risk of therapeutic failure. However, when patients develop AKI, dose reduction should be performed. Despite these data, pharmacokinetic studies in patients with renal impairment are still needed to validate the consensus recommendations.[8]

Conclusion

The occurrence of kidney injury was classified in most patients as stage 1 and with relevant frequency. However, attention and precaution should not be disregarded, with monitoring of renal function being essential, since many of these patients use multiple medications considered as risk factors for causing AKI.

Most deaths in the clinical outcome were related to multidrug-resistant infection when compared to causes due to complications of other comorbidities. Nevertheless, it is difficult to determine whether microbial resistance was the determining factor for the outcome of death, given that these are ICU patients with severe conditions and complex underlying diseases.

Treatment with polymyxin B and broad-spectrum antibiotics should be evaluated with caution, prioritizing the identification of the etiological agent and the sensitivity profile, in order to avoid empirical therapy and prolonged use.

Study limitations

The limitations include the fact that this was a retrospective and single-center study, and the clinical parameters used for outcome assessment, which may be influenced by the professional who recorded them in the medical chart. The use of antimicrobials in combination with polymyxin B limits the isolation of adverse reactions and clinical outcomes caused exclusively by the drug.

Research Ethics Committee approval statement

The present study was developed in accordance with Resolution No. 466 of December 12, 2012, respecting the referential principles of bioethics and ensuring the rights and duties inherent to research participants, the scientific community, and the State. It also complied with the applicable standards for research in human sciences under Resolution No. 510 of April 7, 2016, and met the ethical requirements for research within the scope of the Unified Health System (SUS) under Resolution No. 580 of March 22, 2018. Data collection began only after evaluation and approval by the Ethics Committee of Maternidade Climério de Oliveira - UFBA. The data will be stored for a period of five years in possession of the researchers and subsequently destroyed. As this was a retrospective observational study of secondary data, in which the research participants were hospitalized in the ICU and are no longer hospitalized, making contact impossible, a waiver of the Informed Consent Form (ICF) was requested.

Authors' contributions
JC: Conceptualization and project design; Drafting of the article; Responsibility for all aspects of the text to ensure the accuracy and integrity of any part of the work. JC and PMS: Data analysis and interpretation. PMS and NCABS: Review and editing of the article; Final approval of the version to be published.

Conflicts of interest
The authors of the manuscript entitled Evaluation of Clinical Outcomes in Pediatric Patients Using Polymyxin B declare that there are no conflicts of interest of personal, commercial, academic, political, and/or financial nature in the evaluation and publication process of the referred article.

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I, Jocasta da Costa, declare for the record that the article entitled Evaluation of Clinical Outcomes in Pediatric Patients Using Polymyxin B, for which I am the responsible researcher, has self-funding.

Data availability statement
The underlying contents of the research text are contained within the manuscript.

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References

1. Velkov T, Thompson PE, Azad MA, et al. History, chemistry and antibacterial spectrum. Advances in Experimental Medicine and Biology. 2019;15-36 p. doi: 10.1007/978-3-030-16373-0_3
2. Paterson DL, Bonomo RA. Multidrug-resistant gram-negative pathogens: The urgent need for 'old' polymyxins. Advances in Experimental Medicine and Biology. 2019;9-13 p. doi: 10.1007/978-3-030-16373-0_2
3. Li J. Reviving Polymyxins: Achievements, Lessons and the Road Ahead. Advances in Experimental Medicine and Biology. 2019;1-8 p. doi: 10.1007/978-3-030-16373-0_1
4. Medina E, Pieper DH. Tackling Threats and Future Problems of Multidrug-Resistant Bacteria. Current Topics in Microbiology and Immunology. 2016;3-33 p. doi: 10.1007/82_2016_492
5. Siddiqui NR, Qamar FN, Jurair H, et al. Multidrug resistant gram negative infections and use of intravenous polymyxin B in critically ill children of developing country: retrospective cohort study. BMC Infectious Diseases. 2014;28;14(1). doi: 10.1186/s12879-014-0626-9
6. Downes KJ, Hayes M, Fitzgerald JC, et al. Mechanisms of antimicrobial-induced nephrotoxicity in children. Journal of Antimicrobial Chemotherapy. 2019;75(1):1-13. doi: 10.1093/jac/dkz325 [cited 2022 May 19]
7. KDIGO 2024. Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International. Available from: https://www.kidney-international.org/article/S0085-2538(23)00766-4/fulltext
8. Tsuji BT, Pogue JM, Zavascki AP, et al. International Consensus Guidelines for the Optimal Use of the Polymyxins: Endorsed by the American College of Clinical Pharmacy (ACCP), European Society of Clinical Microbiology and Infectious Diseases (ESCMID), Infectious Diseases Society of America (IDSA), International Society for Anti-infective Pharmacology (ISAP), Society of Critical Care Medicine (SCCM), and Society of Infectious Diseases Pharmacists (SIDP). Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2019;39(1):10-39 p. doi: 10.1002/phar.2209
9. Mattos KPH, Gouvea IR, Quintanilha JCF, et al. Polymyxin B clinical outcomes: A prospective study of patients undergoing intravenous treatment. Journal of Clinical Pharmacy and Therapeutics. 2019;44(3):415-9. doi: 10.1111/jcpt.12801
10. Chiotos K, Tamma PD, Flett KB, et al. Multicenter Study of the Risk Factors for Colonization or Infection with Carbapenem-Resistant Enterobacteriaceae in Children. Antimicrobial Agents and Chemotherapy. 2017;61(12). doi: 10.1128/AAC.01440-17
11. Tjon J, Teoh CH. Medication-Induced Nephrotoxicity in Children. Current Pediatrics Reports. 2020;8(3):122-33 p. Available from: https://link.springer.com/article/10.1007/s40124-020-00223-8
12. Louzada CF, Ferreira AR. Evaluation of the prevalence and factors associated with acute kidney injury in a pediatric intensive care unit. Jornal de Pediatria. 2020;97(4):426-432 p. doi: 10.1016/j.jped.2020.08.003
13. Ferreira MCR, Lima EQ. Impacto do desenvolvimento de lesão renal aguda em pacientes internados na unidade de terapia intensiva pediátrica. Jornal de Pediatria. 2020;96(5):576-81 p. Available from: https://www.scielo.br/j/jped/a/VWWRhFyZWj6sTVwns855pTK/abstract/?lang=pt&format=html