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Artículos originales

Reduction of antimicrobial treatment time in intensive care units in Fortaleza, Brazil

Reducción del tiempo de tratamiento antimicrobiano en unidades de cuidados intensivos en Fortaleza, Brasil

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Resumen

Objetivo: Evaluar la aplicación de la estrategia reducción del tiempo de tratamiento Antimicrobiano (ATM) en Unidades de Cuidados Intensivos (UCI) en un Programa Stewardship de Antimicrobiano (ASP).

Método: Este es un estudio descriptivo y transversal, realizado en dos UCI de un hospital universitario de Fortaleza, Brasil, de enero/2017 a enero/2019. Se incluyeron pacientes adultos, acompañados por un farmacéutico y utilizando ATM, en los que se aplicó la estrategia de reducción del tiempo de tratamiento. La evaluación de la estrategia se realizó a través de la diferencia entre el tiempo previsto establecido al inicio del tratamiento y los días efectivos de uso de cada ATM.

Resultados: De los 100 pacientes incluidos, 51,0 % eran del sexo masculino y 64,0 % ancianos. El sistema respiratorio fue el más frecuentemente afectado (37,4 %) y las clases de ATM más prevalentes fueron los carbapenémicos (23,0 %) y los glicopéptidos (20,1 %). Hubo una disminución de 831 días innecesarios de terapia antimicrobiana y de un promedio de 13,7 a 8,9 días de tratamiento. Las mayores reducciones en días se observaron para meropenem, con 202 días reducidos. El estudio también permitió identificar asociaciones entre la reducción > 8 días de tratamiento y las variables estancia > 22 días y pacientes en cuidados paliativos exclusivos; y asociaciones entre alta hospitalaria y reducciones de hasta 7 días de terapia.

Conclusiones: Los datos obtenidos sugieren que la presencia de un ASP influye en las prácticas de uso de ATM y su tiempo de tratamiento y enfatizan el papel de los profesionales farmacéuticos en estos programas.

Palabras clave: Antibacterianos; Programas de Optimización del Uso de los Antimicrobianos; Cuidados Críticos, Utilización de Medicamentos.

Abstract

Objective: To evaluate the application of the Antimicrobial (ATM) treatment time reduction strategy in Intensive Care Units (ICU) in an Antimicrobial Stewardship Program (ASP).

Method: This is a descriptive and cross-sectional study, carried out in two ICU of a university hospital in Fortaleza, Brazil, from January/2017 to January/2019. Adult patients were included, accompanied by a pharmacist, and using ATM, in which the treatment time reduction strategy was applied. The evaluation of the strategy was made through the difference between the predicted time established at the beginning of the treatment and the effective days of use of each ATM.

Results: Of the 100 patients included, 51.0 % were male and 64.0 % were elderly. The respiratory system was the most frequently affected by the infections (37.4 %) and the most prevalent classes of ATM were carbapenems (23.0 %) and glycopeptides (20.1 %). There was a decrease from 831 unnecessary days of antimicrobial therapy and from an average of 13.7 to 8.9 days of treatment. The greatest reductions in days were observed for meropenem, with 202 days reduced. The study also allowed the identification of associations between the reduction > 8 days of treatment and the variables length of stay > 22 days and patients in exclusive palliative care, and associations between hospital discharge and reductions of up to 7 days of therapy.

Conclusions: The data obtained suggest that the presence of an ASP influences the practices of ATM use and its treatment time and emphasize the role of pharmaceutical professionals in these programs.

Keywords: Anti-Bacterial Agents; Antimicrobial Stewardship; Critical Care; Drug Utilization.

Highlights

The Antimicrobial Stewardship Program (ASP) has been considered as a way towards the rational use of antimicrobials (ATM), especially in ICU. Further, ASP is widely used to reduce exposure to ATMs. However, in Brazil, studies that evaluate the impact of ASP in the ATM management of ICUs are still scarce.

This study found that the duration of treatment in patients taking ATM in ICUs significantly correlate with length of stay, exclusive palliative care and hospital outcome.

These findings reinforce the importance of an ASP in hospital settings for modulating antimicrobial use practices and optimizing their use for reduction of treatment duration.

Introduction

Antimicrobials (ATM) are among the most widely used drugs in the world.[1] Their development enabled important progress in the history of medicine and a change in the prognosis of infections. However, the emergence of resistant microorganisms and the significant decrease in the effectiveness of ATM currently represent one of the most serious public health concerns worldwide, making the rational use of these drugs urgent.[2]

The World Health Organization (WHO) warns that without the implementation of control measures, society may enter a "post-antibiotic age".[3] Despite this, it has estimated currently 50 % of ATM prescriptions are considered unnecessary or inappropriate whether due to indication, dosage or even duration of treatment.[4] The indiscriminate use has had an impact on length of stay, hospital costs and on patient morbidity and mortality, in addition to increasing microbial resistance by selective pressure.[5]

In Intensive Care Units (ICU), ATMs are massively used and it has believed that up to 70 % of ICU patients could to receive antimicrobial therapy per day of hospitalization, whether empirical or directed by culture of biological material.[6] Although the empirical use of ATM has an important role in the treatment of patients with sepsis and septic shock in this environment, the high frequency of empirical prescription for prolonged periods without proper laboratory confirmation is observed and may contribute to the emergence of adverse events.[6,7]

In this context, the Antimicrobial Stewardship Program (ASP) has been considered a way towards the rational use of ATMs and better prescription practices in the ICU, through strategies such as de-escalation, sequential oral therapy, reduction of treatment time, among others.[8] The ASP proposes a multidisciplinary approach, it is optimizing antimicrobial therapy and promoting the establishment of a healthy local microbiota that it is sensitive to existing ATMs, the use of ATMs rationally and for an adequate period, and better clinical outcomes. In this Program, pharmaceutical professionals play an important role.[9]

In recent years, ASP programs have helped to consolidate the practice of reducing exposure to ATMs in the scientific community.[4,10] This reduction occurs through the adequacy of treatment from the third day of treatment using the strategy of de-escalation adjusted to the antibiogram and clinical evolution or through early suspension of treatment, when it proves being quickly effective, the patient does not have severe immunosuppression and there is not a particularly difficult-to-treat microorganism.[11] However, despite the benefits of reducing the duration of treatment antimicrobials in clinical, microbiological and economic terms, adherence to shorter therapies is still a major gap, even when their extension does not bring an additional benefit to the patient's clinical condition.[12]

In Brazil, the studies that evaluate the effects of an ASP in the management of ATM in intensive care are scarce, especially with focus on reducing the time of antimicrobial treatment.[13] Thus, this work aims to evaluate the reduction of unnecessary days of antimicrobial therapy through the application of the treatment time reduction strategy in the ICU environment of a university hospital that has an ASP led by pharmacists.

Methods

This is a descriptive and cross-sectional study, with a quantitative approach, carried out in a clinical ICU and a post-surgical ICU of a public university hospital in Fortaleza, Ceará, Brazil, from January/2017 to January/2019. The study was approved by the institution's ethics and the research committee with number 2945868 and carried out considering respect for human dignity.

The study hospital is a unit that provides high complexity health care in the State of Ceará and integrated into the Unified Health System (SUS). The institution has one clinical ICU and one postsurgical ICU, each with 8 active beds. The multidisciplinary team at the ICU is composed of physicians on duty and a day laborer, nurses, physiotherapists, a nutritionist, and a clinical pharmacist. There are also resident professionals in the field of medicine, nursing, pharmacy, and physiotherapy. The institution under

study did not have a prescription system and/or electronic evolution during the study, nor did it have its own inpatient unit for patients in Exclusive Palliative Care (EPC).

The studied population included patients from 18 years of age, with a minimum length of stay in the ICU of 48 hours, accompanied by an intensive care pharmacist and using strategic and reserve ATMs in which the treatment time reduction strategy was applied. Patients whose suggestion to reduce treatment time was not applied by the medical care team and those with duplicate or incomplete data were excluded. Patients aged 60 years or older were classified as elderly, according to Law 10,741 of 2003, in force in Brazil.[14]

Patient data were collected from medical records and duplicates of drug prescriptions filed in the pharmacy sector. Demographic and clinical variables collected from patients included gender, age, reason, and length of stay in the ICU, comorbidities, prescribed antimicrobial, with their respective indications for use, systems affected by the infections, expected days of treatment and days of use, previous hospitalization within 30 days and hospital outcome. It was also collected if the patient is in exclusive palliative care or not.

The identification of patients with criteria for the application of the treatment time reduction strategy was carried out by the ASP team, which is an institutionalized program since 2017 in the ICUs and in some care units. In the program, an infectious disease specialist from the CCIH meets weekly at the bedside with the multidisciplinary team of each ICU to discuss the clinical and laboratory evolution of patients and define the best therapeutic strategies for antimicrobial therapy.

The treatment time reduction strategy is described as the difference between the days of use of each antimicrobial in relation to the time expected at the beginning of the treatment, according to the institutional protocol and the patient's clinical condition. To apply this strategy, it was necessary to confirm the patient's clinical and laboratory improvement after at least 72 hours of treatment. For that purpose, clinical parameters were evaluated, such as the absence of fever, hemodynamic stability, normalization of the leukogram and reduction in the levels of infection biomarkers. In this study, the reduced treatment time was divided into two arbitrary groups: reduction of up to 7 days and reduction of from 8 days of treatment.

Strategic antimicrobials were those that are part of the institution's standardization and are likely to perform sequential oral therapy because they have oral bioavailability greater than 80 %, namely: ciprofloxacin, levofloxacin, metronidazole, fluconazole, clindamycin, voriconazole. Those with a broad spectrum and/or high cost were considered as reserve antimicrobials, namely, piperacillin/tazobactam, meropenem, ertapenem, polymyxin B, polymyxin E (colistin), tigecycline, vancomycin, teicoplanin, linezolid, daptomycin, micafungin, anidulafungin, voriconazole, amphotericin B lipid and liposomal complex. The system affected by the infection were classified according to the indication for treatment through standardization of the service carried out by the infectious disease specialist and pharmacists of the ASP team. To exemplify, for the indication pneumonia, the system affected by the infection is the respiratory; for septic shock, it is blood. The ATMs involved in the recommendations were classified by the second level of the Anatomical Therapeutic Chemical (ATC).[15]

The collected data were entered and evaluated using Excel® Software, version 2016. Numerical variables were presented as mean and standard deviation and categorical variables were displayed in frequency to investigate the factors associated with the acceptance of pharmaceutical recommendations. A significance level of 5 % was adopted. In investigating the association between the variables, Fisher's exact test was performed in the statistical program Graph Pad Prism 6, version 6.07 (USA). The methodological flow of the study is summarized in Figure 1.

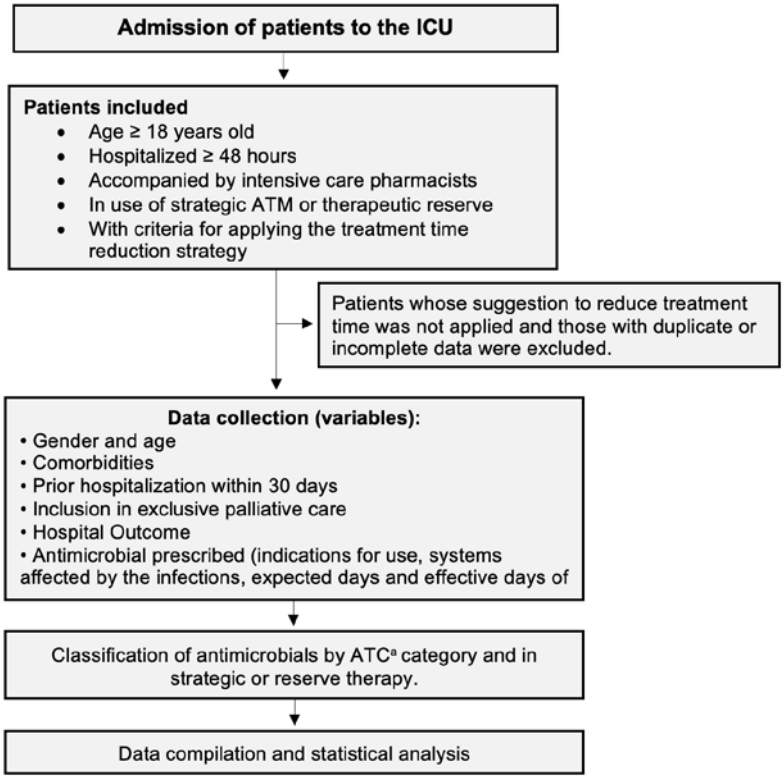

Figure 1. Methodological flow of the study on the reduction of antimicrobial treatment time and hospitalized patients in intensive care units environments of a university hospital in Fortaleza (January/2017 to January/2019). [a]ATC: *Anatomical Therapeutic Chemical.*

Results

During the study, 103 patients admitted to the ICU met the inclusion criteria. However, two were excluded because the treatment time reduction strategy was not applied, and one was excluded due to incomplete and duplicate data. Regarding the demographic profile, 51.0 % of the patients were male, 64.0 % were elderly and 8 % were in EPC (Table 1). The mean age was approximately 59 years ± 17.9, ranging from 18 to 89 years.

Most patients had at least one comorbidity (85.0 %), the most frequent being systemic arterial hypertension (44 %), diabetes mellitus (24 %) and renal dysfunction (12 %). As for the type of care, most patients were admitted to the clinical ICU (59.0 %) and had a hospital stay of more than 22 days (47.7 %). The mortality rate in the ICU was 42.0 % (Table 1). The mean length of hospital stay was 47 ± 34.7 days, ranging from 5-185 days. A 63 % of patients had previous hospitalization of up to 30 days before the current hospitalization.

To better characterize the treatment time reductions in this study, a statistical analysis was performed between the demographic and clinical variables of the patients and the time reduction categories (up to 7 days and more than 7 days). The test showed a statistically significant association between a reduction of 8 or more days of treatment with length of stay of more than 22 days (p=0.037) and pa-

tients with EPC (p=0.029). In addition, an association was observed between the clinical outcome of discharge and the reduction of up to 7 days of antimicrobial treatment (p=0.002) (Table 1).

Table 1. Demographic and clinical profile of patients (n=100) who had a reduction in antimicrobial treatment time in two ICUs of a university hospital in Fortaleza (January/2017 to January/2019).

Clinical variables	Number of treatments (total=174)	R[a] ≤ 7 days	R[a] > 8 days	p[d]	RR[e]	CI[f]
Gender						
Female (n=49)	81 (46.6 %)	70	11	0.536	1.044	0.919-1.185
Male (n=51)	93 (53.4 %)	77	16			
Age[b]						
Not elderly (n=36)	100 (57.8 %)	88	12	0.144	1.104	0.963-1.264
Elderly (n=64)	74 (42.5 %)	59	15			
Comorbidity[c]						
Yes (n=85)	155 (89.1 %)	131	24	1.000	1.004	0.816-1.233
No (n=15)	19 (10.9 %)	16	3			
Previous hospitalization						
Yes (n=63)	113 (64.9 %)	94	19	0.661	0.957	0.842-1.088
No (n=37)	61 (35.1 %)	53	8			
Inpatient unit						
Clinical ICU (n=59)	103 (59.2 %)	86	17	0.831	0.972	0.855-1.104
Post-surgical ICU (n=41)	71 (40.8 %)	61	10			
Hospital length of stay						
≤ 7 days (n=19)	28 (16.1 %)	24	4	1.000	1.017	0.861-1.202
8 – 14 days (n=26)	37 (21.3 %)	35	2	0.072	1.157	1.036-1.292
15 – 21 days (n=20)	26 (14.9 %)	23	3	0.770	1.056	0.903-1.234
>22 days (n=35)	83 (47.7 %)	65	18	0.037	0.869	0.761-0.991
Exclusive palliative care (EPC)						
Yes (n=8)	17 (9.8 %)	11	6	0.029	0.747	0.523-1.067
No (n=92)	157 (90.2 %)	136	21			
Clinical outcome						
Hospital discharge (n=58)	124 (71.3 %)	112	12	0.002	1.290	1.067-1.561
Death (n=42)	50 (28.7 %)	35	15			

[a]Reduction. [b]In Brazil, the elderly are individuals aged 60 years or older. [c]At least one comorbidity. [d]p: Fisher's exact test; p<0.05. [e]RR: relative risk. [f]CI 95 %: confidence interval of 95 %.

A total of 174 ATM treatment reductions were evaluated, involving nine different systems affected by the infection. The most frequent system in treatment reductions were respiratory (37.4 %; n=65), blood (27.0 %; n=47) and indeterminate (13.2 %; n=23). On the other hand, the least frequent system were surgical wounds (1.5 %; n=2), bone and joint wounds (1.5 %; n=2) and central nervous system (0.6 %; n=1) (Table 2).

It totals of 15 different ATMs were involved in the recommendations, with 83.3 % (n=145) of the ATMs being therapeutic reserve and 14.4 % being considered strategic. The therapeutic classes, there was a prevalence of Carbapenems (23.0 %; n=40), Glycopeptides (20.1 %, n=35), Penicillin combinations, incl. beta-lactamase inhibitors (14.9 %, n=26), being meropenem (23.0 %; n=40), piperacillin+tazobactam (14.9 %; n=26) and vancomycin (12.6 %; n=22) the main ATMs involved.

The sum of the total number of predicted days of antimicrobial treatment was 2,378 days. The total sum of days of treatment performed was 1,547 days, which represents 831 days reduced in antimicrobial therapy. The overall mean treatment time was reduced from 13.7 ± 4.0 days to 8.9 ± 3.8 days. The greatest reductions in treatment days were seen with meropenem (202 days reduced), vancomycin (114 days reduced), piperacillin+tazobactam (98 days reduced), polymyxin B (88 days reduced), and teicoplanin (55 days reduced) (Table 2).

Table 2. Systems affected by the infections and predicted and effective days of treatment of patients who had a reduction in antimicrobial treatment time in two ICUs of a university hospital in Fortaleza-Ceará (January/2017 to January/2019).

Variables		N (%) Sum	Predicted days		Effective days		Reduced days	
			Average ± SD[a]	Sum	Average ± SD[a]	Sum	Average ± SD[a]	
Systems affected by the infections	Respiratory	65 (37.4)	825	12.7 ± 2.8	559	8.6 ± 2.9	266	4.1 ± 2.6
	Blood	47 (27.0)	648	13.8 ± 3.1	456	9.7 ± 3.7	192	4.1 ± 2.8
	Undetermined	23 (13.2)	306	13.3 ± 2.6	205	8.9 ± 3.5	101	4.4 ± 3.0
	Gastrointestinal	19 (10.9)	297	15.6 ± 4.8	168	8.8 ± 6.1	129	6.8 ± 3.7
	Cutaneous/soft tissues	9 (5.2)	136	15.1 ± 5.0	71	7.9 ± 4.0	65	7.2 ± 5.9
	Urinary	6 (3.4)	76	12.7 ± 2.1	49	8.2 ± 3.7	27	4.5 ± 2.8
	Others[b]	5 (2.9)	90	-	39	-	51	-

Antimicrobials	Meropenem	40 (23.0)	593	14.8 ± 5.4	391	9.8 ± 3.8	202	5.1 ± 5.5
	Piperacillin/ tazobactam	26	312	12.0 ± 2.0	214	8.2 ± 1.8	98	3.8 ± 2.2
	Vancomycin	22	327	14.9 ± 5.6	213	9.7 ± 4.8	114	5.2 ± 4.5
	Polymyxin B	22	308	14.0 ± 3.2	220	10.0 ± 4.7	88	4.0 ± 3.1
	Teicoplanin	13	174	13.4 ± 3.2	119	9.2 ± 3.6	55	4.2 ± 2.8
	Fluconazole	11	157	14.3 ± 2.5	102	9.3 ± 3.7	55	5.0 ± 3.0
	Linezolid	10	124	12.4 ± 2.1	79	7.9 ± 3.8	45	4.5 ± 2.9
	Micafungin	8	108	13.5 ± 1.4	68	8.5 ± 2.3	40	5.0 ± 2.6
	Tigecycline	6	80	13.3 ± 1.6	37	6.2 ± 4.0	43	7.2 ± 3.7
	Levofloxacin	5	66	13.2 ± 1.8	39	7.8 ± 1.6	27	5.4 ± 2.1
	Others[c]	11	129	-	65	-	64	-

[a]SD: standard deviation. [b]Other (Central nervous system, surgical and bone/joint site): systems affected by the infections with a lower frequency of less than 3. [c]Others (anidulafungin, ciprofloxacin, clindamycin, ertapenem and metronidazole): systems affected by the infections with a lower frequency of less than 5.

Discussion

From the researched literature, it is noted that this is one of the first studies to evaluate the reduction of ATM treatment time through an ASP in an adult ICU, in Brazil. This study reinforces the importance of implementing an ASP to optimize therapeutic results and reducing resistance to antimicrobials in an intensive care environment with the leadership of pharmacists.[16,17] Furthermore, it establishes unprecedented associations between the clinical variables analyzed and the reduction of up to 7 or more days of treatment.

ICUs represent an important target for ASPs, since a large proportion of parenteral ATM use, especially broad-spectrum ATMs, and the ATMs are the main drugs prescribed in these units. The presence of many patients with serious and potentially fatal infections makes it vital to apply the fundamentals of ASP, which aim to use the right antimicrobial, at the right time, in the right dose, for the right microorganism and for the right duration.[18] In this scenario, the application of the ASP strategy to reduce treatment time it's essential, as it favors the reduction of the selective pressure of microorganisms and the risk of adverse drug reactions, in addition to promoting a reduction in hospital costs.[7]

In the ICU under study, there was a predominance of male patients (51 %) and elderly patients (64 %), which agrees with other national and international studies that report a similar profile.[19-21] Most patients presented mean long ICU stay (>22 days), previous hospital stays (63 %) and at least one comorbidity (85 %), which may be associated with the high mortality rate found (42 %). In the literature, results of the multicenter study EPIC II (Extented Prevalence of Infection in Unit Care) suggest that there is a relationship between the type of infection, the existence of comorbidity and the increase in the mortality rate, data that could help to understand the clinical profile of the patients in this research.[22] In addition, the presence of patients in exclusive palliative care in this study may help to explain the high mortality rate observed.[23]

The most prevalent systems affected by the infections in the study were respiratory (37.4 %) and blood (27.0 %), corroborating data from the literature, which indicate a higher prevalence of certain infections, such as pneumonia, sepsis and bloodstream infections, in ICUs in Brazil.[22] The observed high frequency of infections of undetermined focus is also reported in scientific studies, since empiric,

broad-spectrum therapy and started immediately is essential to reduce mortality in patients with sepsis or shock septic.[24-26] However, early administration of ATM should be done with a commitment to avoid unnecessary use and to promote therapy de-escalation, especially for broad-spectrum agents and in the absence of proven infection.[27]

Regarding treatment time, an average reduction from 13.7 to 8.9 days was observed, representing a decrease of approximately 36.4 % in ATM use. Similar time reduction from 14.1 to 11.9 days was reported in the study by Brahmi *et al.* (2006), carried out in an ICU in Tunisia.[28] In another study developed in Greece, the consumption of restricted and general ATMs was reduced by 92.5 % and 55.4 %.[29] Other studies that used the strategies of the ASP have reported a reduction in unnecessary ATM prescribing from 38 % to 11 % through the Defined Daily Doses (DDD) tool, which includes reducing use due to discontinuation of treatment and due to adjustment of doses for kidney/liver function.[30-33]

According to the literature, the ideal time for treatment with ATM is the shortest possible time, without compromising efficacy, and it varies according to the infectious focus, the initial clinical response and the microbiological results.[34] In recent decades, the duration of antimicrobial therapies has significantly decreased due to the fact that long-term therapies lead to colonization of pathogenic microorganisms, development of multidrug-resistant organisms and recurrent infectious episodes. Additionally, studies support the reduction of antimicrobial therapy for bacterial infections, both community and hospital acquired, in the absence of multidrug-resistant pathogens and when appropriate therapy generates an adequate response within the first six days.[35-38]

In this research, broad-spectrum and therapeutic reserve ATMs were the most involved in treatment time reductions. Meropenem (23.0 %), piperacillin/tazobactam (14.9 %) and vancomycin (12.6 %) stood out, representing the classes of carbapenems, glycopeptides and cephalosporins, respectively. In the study by Panagiotis *et al.* (2007), who evaluated the overall impact of implementing an ASP in an ICU in Greece, observed a reduction in the use of carbapenems by 22.7 % and piperacillin/tazobactam by 38.1 %.[29] In the study by a López-Vinau *et al.* (2021), the development of a package of educational and restrictive measures within an ASP proved to be effective and safe not only in reducing the use of carbapenems, but also in decreasing carbapenem-resistant Gram-negative bacilli.[39]

In clinical practice, carbapenems are ATM active especially against Gram-negative bacteria and are widely used in nosocomial infections to treat infections caused by multidrug-resistant microorganisms, especially in the care of critically ill patients.[40] The high consumption of meropenem is related to the growth of bacilli Gram-negative resistant to β-Lactam antibiotics in ICU patients, and ASP initiatives for their optimization may be useful to limit the emergence of multidrug-resistant microorganisms, in addition, the rational use of carbapenems can reduce the prevalence of adverse effects related to the prolonged use of ATMs, such as *Clostridium difficile* infections.[41,42]

About vancomycin, it is believed that this was one of the ATMs that showed the greatest reduction in treatment time, due to its high empirical use when there is suspicion of life-threatening Gram-positive infections. One of the main indications for the use of vancomycin is suspected or confirmed nosocomial infection with methicillin antibiotic-resistant staphylococci (MRSA) and sensitive *Enterococcus faecium*, which are rare infections. This empirical treatment initiation may lead to the inappropriate use of vancomycin and promote the reduction of treatment time within a few days after starting therapy.[43,44]

In our research, an association was observed between a reduction in treatment time > 8 days and two variables: length of stay >22 days (p=0.037) and patients in EPC (p=0.029). These results seem to be interconnected, since the patients who entered EPC were possibly chronically critical patients (considering the profile of ICU patients) who had a prolonged hospital stay, without resolution of the clinical condition and with an expected treatment time greater than 10 or 14 days. Furthermore, when defining EPC for a patient at the institution under study, it is generally decided to proceed with the early suspension of ATM, regardless of the length of treatment completed. Thus, a greater reduction in days of ATM treatment is observed in patients with EPC and is not necessarily related to a clinical improvement of the infection.

Additionally, it was found that the outcome of ICU discharge was related to reductions of up to 7 days of therapy (p=0.002). Regarding this result, it is believed that patients who were discharged from the

ICU had less severe clinical conditions and shorter ATM treatment time predictions, up to 7 or 10 days. These predictions would come true and would lead to the cure of the patient and his subsequent discharge from the ICU, often. Thus, it is also assumed that reductions in fewer days of treatment were associated with more assertive predictions of the treatment time required for the patient to cure.

Our study has some limitations. Firstly, these results cannot be extrapolated to all types of hospitals, institutions without a clinical pharmacist, neither to non-adult ICU populations or to hospitals that do not have an institutionalized ASP. Secondly, this is a single-center study that did not assess the impacts of interventions on clinical outcomes or costs and did not show a reduction in the use of ATMs by the DDD unit, which made it difficult to compare results. Furthermore, we did not exclude chronic critical patients in EPC, in whom the duration of antimicrobial therapy was reduced by prioritizing comfort measures and not by better clinical response. However, we evaluated the application of a strategy to reduce treatment time in two ICUs in Fortaleza, expanding the dissemination of the strategy and reinforcing its importance. Future research should explore these issues in other health centers.

Conclusion

The main finding of this research was the decrease of 831 unnecessary days of antimicrobial therapy and from an average of 13.7 to 8.9 days of treatment. The main antimicrobials involved were broad-spectrum and considered therapeutic reserve, with emphasis on meropenem. Additionally, the study allowed the identification of associations between the reduction > 8 days of treatment and the variables length of stay > 22 days and patients in exclusive palliative care. The hospital discharge outcome was also associated with reductions of up to 7 days of therapy. The data obtained suggest that the presence of an Antimicrobial Stewardship Program influences antimicrobial use practices and is effective in optimizing their use, in addition to reinforcing the leadership of the Programs by pharmaceutical professionals.

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