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Antimicrobial consumption in a hospital environment before and after restrictive commercialization measures in Brazil

Consumo de antimicrobianos em ambiente hospitalar antes e após medida restritiva de comercialização no Brasil

Consumo de antimicrobianos en ambiente hospitalario antes y después de medidas restrictivas de comercialización en Brasil

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ABSTRACT

Introduction: The consumption of antimicrobials (ATB) has been described as one of the causes of Bacterial Resistance. In 2010, RDC 44 was published in Brazil, which restricts the free sale of ATB to reduce antimicrobial resistance in hospitals. **Aim:** to identify the consumption of ATB in a teaching hospital before and after the implementation of the restrictive measure on the commercialization of antimicrobials in Brazil. **Outlining:** Cross-sectional study carried out in a general hospital. Analyzes were carried out in two phases, using the variables ATB consumption, expressed in defined daily dose (DDD), average use of different ATB per patient and the frequency of resistant microorganisms in the period. **Results:** The average use of ATB per patient was 2.56 (Standard Deviation (SD) ± 2.02) and 2.40 (SD ± 1.89) in phases I and II, respectively (p=0.0007). The general variation in defined daily dose was 1.89%, however drugs with negative variation were observed. A higher frequency of resistant microorganisms isolated in phase I was observed compared to phase II (OR=1.48, CI: 1.13-1.93, respectively). **Implications:** A difference was identified in the consumption of ATB between the periods, with an increase in general consumption, in DDD, but a lower average number of different ATBs per patient and a lower occurrence of resistant microorganisms.

DESCRIPTORS

Anti-Infective Agents; Drug Resistance; Pharmacovigilance; Drug Utilization.

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INTRODUCTION

Excessive consumption of antimicrobials has been extensively described in the literature as one of the main causes of Bacterial Resistance (BR).[1-4] BR can reduce the effectiveness of antimicrobials and cause harm to the patient and burden health systems.[5]

Issues related to the use of antimicrobials and BR have a major impact on public health, which is why the global action plan of the World Health Organization (WHO) has among its main objectives the optimization of the use of antimicrobials.[1] Despite efforts, a growing prevalence of RB has been identified worldwide, especially in developing countries.[6]

The creation of national regulatory agencies, the implementation of political measures for the control, the provision of continuing education for health professionals and the strengthening of health units are prevention strategies.[7]

In Brazil, the collegiate board of the National Health Surveillance Agency (Anvisa), through RDC 44, published on October 28, 2010, in its Article 2, determined that drugs containing antimicrobials sold under medical prescription could only be dispensed using special control prescriptions, with a view to restricting access to these drugs and minimizing the occurrence of BR.[8] This resolution was revoked by RDC 20, of May 5, 2011, which covers the same topic and is still in force today.[9]

Some studies point to the contributions of restrictive measures in the consumption of antimicrobials in pharmacies and drugstores,[10-11] as well as in reducing resistance in the community and hospital setting.[12] Furthermore, studies indicate that rationalization of use is necessary so that the strategies implemented are effective.[13] Considering that the consumption of antimicrobials impacts BR, the need to evaluate their consumption in the hospital setting is identified.

This article aims to identify the consumption of antimicrobials in a teaching hospital before and after the implementation of the restrictive measure on the commercialization of antimicrobials in Brazil.

METHOD

Study outlining and setting

The study comprises two cross-sectional analyzes with adult patients admitted to a hospital from May to October 2010 (Phase I) and February to July 2011 (Phase II), before and after the restrictive measure on the commercialization of antimicrobials. The study was carried out in a general public hospital, linked to teaching and research, which has around 330 beds, being a reference for the northern region of Belo Horizonte and neighboring municipalities.

Patients over 18 years of age who had antimicrobial dispensing identified by institution's electronic medication tracking system were included. The following were excluded: Patients diagnosed with bacterial infection at the time of admission or up to 72 hours after hospital admission; female patients admitted for childbirth and postpartum period; patients transferred from another hospital or with a hospital stay of less than 72 hours and patients for whom culture tests were requested by swab collection, for the purpose of identifying colonization.

During the periods analyzed, no changes were observed in the clinical staff and team responsible for controlling infections associated with the institution's health care. There were also no shortages in the supply of drugs or changes in the standardization of procedures involving the institution's examinations.

Study variables

The overall consumption of prescribed antimicrobials, expressed in defined daily dose (DDD), was considered as outcome variable in the two analysis periods (Phases I and II). The evaluated antimicrobials comprise drugs for systemic use which are in the marketing list under special control with DDD established by the WHO. Antimicrobials for

non-systemic use (topical, rectal, vaginal and ophthalmological), without definition of DDD by the WHO and those whose dispensing was not changed by the restrictive measure, such as fluconazole, nystatin and ketoconazole were not considered.

The variables studied were gender, age, average length of stay (in days) and identification of a positive culture test result for BR in the period.

This study considers BR as the resistance to antimicrobials from a clinical point of view and a resistant result on the antibiogram, considering a greater probability of therapeutic failure when an infection caused by a certain microorganism is treated with a class of antimicrobials usually used in clinical practice.[14]

Source, collection and analysis of data

Information about antimicrobials in use was collected from secondary data, through computerized report generation. Antimicrobial dispensing data was collected through the traceability system of pharmacy of the institution. In this report, drugs not administered to patients and those counted as returns were excluded.

The drugs were classified according to the Anatomical Therapeutic Chemical (ATC).[15] The consumption was expressed as DDD per 1000 patient-days, considering the DDD of each antimicrobial during the study period in accordance with the standard DDD established by the WHO.[15] The calculation comprised the ratio of the total amount used in grams of antimicrobial in the period to the standard DDD established by the WHO, over the total population in the period and location, multiplied by 1000.[15]

The occurrence of BR was also identified in culture tests for patients who used antimicrobials. BR was evidenced by the generation of a report from the institution's outpatient clinic, in which positive results from *in vitro* culture of microorganisms and results from the *in vitro* sensitivity test to antimicrobials (STA, antibiogram) were interpreted as "resistant". For this identification, results from blood culture, urine culture and various tissue cultures were considered.

The data were entered into an Excel spreadsheet to perform descriptive statistics. Absolute and relative frequencies were obtained for categorical variables, and measures of central tendency and dispersion were obtained for interval quantitative variables. The chi-square test was used to compare the proportions of categorical variables (age, length of stay and quantity of antimicrobials used were stratified according to their distribution).

Continuous variables were compared using the Student's t test or the Wilcoxon-Mann Witney test, when applicable. Logistic regression was used to estimate odds ratios (OR), considering a 95% confidence interval (95%CI) to investigate the association between explanatory variables and the outcome. A significance level of 0.05 was adopted, according to the Wald chi-square test. The SAS® 9.4 software was used to carry out the analyses.

Ethical Considerations

The project was approved by the Human Research Ethics Committee of the Federal University of Viçosa (Official Letter 176/2012).

RESULTS

A total of 5,317 patients were included in the study, 2,644 in phase I and 2,673 in phase II. In both phases there was a greater predominance of males (approximately 64.0% in phases I and II). The median age in phase I was 50 years, distributed in the interquartile range 32 years in the first quartile and 69 years in the third quartile. In phase II, the median age was 49 years old, with the result being 31 years old in the first quartile and 68 years old in the third quartile.

Regarding length of hospital stay (LHS), the median in phase I was seven days, with the first quartile of two days and the third quartile of 15 days. In phase II, the median of LHS was six days, the first

quartile was two days, and the third quartile was 17 days. No statistically significant differences were observed between these variables. In relation to patients who were readmitted, there was a higher proportion in individuals in phase I (11.12% versus 8.75%), p=0.0039. As to the use of antimicrobials, it was observed that in phase I patients used an average of 2.56 (Standard Deviation (SD) ± 2.02) different antimicrobials, while in phase II the average use was 2.40 (SD ± 1.89), with a statistically significant difference between the groups (p=0.0007).

Antimicrobial consumption was analyzed according to dispensing for each patient and consumption by calculating the defined daily dose (DDD) per 1,000 patients/day. A percentage variation of +1.89% was obtained considering all antimicrobials between phases. When analyzing the consumption of each antimicrobial, a negative variation was observed in the consumption of amikacin, amphotericin B, levofloxacin and teicoplanin, among others, and a positive variation in drugs such as linezolid, ciprofloxacin, metronidazole and cefepime (Tables 1a and 1b), in which the following acronyms were used: Amikacin – Amika; Gentamicin – Gen; Amphotericin B – Ampho B; Cephalexin – Cephale; Cefazolin – Cefaz; Cefepime – Cefe; Cefotaxime – Cefo; Ceftazidime – Cefta; Ceftriaxone – Ceftr; Nitrofurantoin – Nitro; Metronidazole – Metro; Ciprofloxacin – Cipro; Levofloxacin – Levo; Norfloxacin – Nor; Teicoplanin – Teico; Vancomycin – Vanco; Clarithromycin – Clari; Clindamycin – Clinda; Linezolid – Line; Amoxicillin + Clavulanic Acid - Amox + Clav; Ampicillin + Sulbactam – Amp + Sulb; Piperacillin + Tazobactam – Pipe + Tazo; Amoxicillin – Amox; Ampicillin – Amp; Benzylpenicillin Benzathine - Benzyl B; Polymyxin B - Poly B; Sulfamethoxazole + Trimetropin – Sulfa + Tri; Sulfadiazine – Sulfa.

Table 1a - Specification of antimicrobial consumption (average consumption per patient) in the study phases.

Pharmacological class	Drug	Route of administration	Phase I N (%)	Phase II N (%)
Aminoglycosides	Amika	Parenteral	133 (2.04)	100 (1.49)
	Gen	Parenteral	428 (6.55)	430 (6.41)
Antimycotic-antibiotics	Ampho B	Parenteral	13 (0.20)	19 (0.28)
Carbapenems	Metro	Parenteral	215 (3.29)	280 (4.17)
Cephalosporins	Cephale	Oral	24 (0.37)	21 (0.31)
	Cefaz	Parenteral	1446 (22.14)	1662 (24.78)
	Cefe	Parenteral	133 (2.04)	205 (3.06)
	Cefo	Parenteral	37 (0.57)	27 (0.40)
	Cefta	Parenteral	48 (0.74)	92 (1.37)
	Ceftr	Parenteral	545 (8.35)	481 (7.17)
Nitrofurantoin-derived	Nitro	Oral	7 (0.11)	14 (0.21)
Imidazole-derived	Metro	Oral	59 (0.90)	79 (1.18)
	Metro	Parenteral	503 (7.70)	499 (7.44)
Fluoroquinolones	Cipro	Parenteral	118 (1.81)	166 (2.47)
	Cipro	Oral	147 (2.25)	166 (2.47)
	Levo	Oral	53 (0.81)	36 (0.54)
	Levo	Parenteral	35 (0.54)	29 (0.43)
	Nor	Oral	74 (1,13)	70 (1.04)
Glycopeptides	Teico	Parenteral	36 (0.45)	32 (0.48)
	Vanco	Parenteral	283 (4.33)	308 (4.59)

Lincosamides	Clinda	Parenteral	181 (2.77)	161 (2.40)
	Clinda	Oral	27 (0.41)	22 (0.33)
Macrolides	Clari	Oral	130 (1.99)	72 (1.07)
Other antibacterials	Line	Parenteral	2 (0.03)	1 (0.01)
Penicillin + Beta-lactamase inhibitors	Amox+Clav	Parenteral	580 (8.88)	558 (8.32)
	Amox+Clav	Oral	343 (5.25)	318 (4.74)
	Amp+Sulb	Parenteral	73 (1.12)	64 (0.95)
	Pipe+Tazo	Parenteral	319 (4.89)	220 (3.28)
Extended-spectrum penicillins	Amox	Oral	49 (0.75)	37 (0.55)
	Ampi	Parenteral	77 (1.18)	77 (1.15)
Beta-lactamase resistant penicillins	Oxa	Parenteral	216 (3.31)	215 (3.21)
Beta-lactamase sensitive penicillins	Benzil B	Parenteral	3 (0.05)	1 (0.01)
Polymyxins	Poli B	Parenteral	156 (2.39)	202 (3.01)
Sulfonamides + Trimetropin	Sulfa+Tri	Oral	29 (0.44)	37 (0.55)
Intermediate-acting sulfonamides	Sulfa	Oral	8 (0,.12)	7 (0.10)

Caption: Clarithromycin – Clari; Cefepime – Cefe; Ceftriaxone – Ceftr; Cirpofloxacin – Cipro; Ampicillin – Amp; Amphotericin B – Ampho B; Sulfadiazine – Sulfa; Benzylpenicillin Benzathine - Benzyl B; Metronidazole – Metro; Linezolid – Line.
Source: Prepared by the authors.

Table 1b - Specification of antimicrobial consumption (consumption per DDD/1000 patient-days) in the study phases.

Pharmacological class	Drug	Route of administration	Phase I	Phase II
Aminoglycosides	Amika	Parenteral	9.64	8.16
	Gen	Parenteral	12.28	13.43
Antibiotic-antimycotic	Ampho B	Parenteral	3.36	1.72
Carbapenems	Metro	Parenteral	13.77	19.58
Cephalosporins	Cephale	Oral	0.39	0.33
	Cefaz	Parenteral	17.92	20.55
	Cefe	Parenteral	3.17	6.90
	Cefo	Parenteral	1.42	1.00
	Cefta	Parenteral	2.47	4.72
	Ceftr	Parenteral	52.78	48.80
Nitrofurantoin-derived	Nitro	Oral	0.35	0.50
Imidazole-derived	Metro	Oral	0.72	1.11
	Metro	Parenteral	16.49	16.71
Fluoroquinolones	Cipro	Parenteral	2.30	3.86
	Cipro	Oral	3.79	4.82
	Levo	Oral	4.00	2.66
	Levo	Parenteral	2.86	2.20

	Nor	Oral	3.89	3.89
Glycopeptides	Teico	Parenteral	2.71	2.19
	Vanco	Parenteral	12.05	12.80
Lincosamides	Clinda	Parenteral	5.65	6.41
	Clinda	Oral	0.79	0.53
Macrolides	Clari	Oral	11.71	5.46
Other antibacterials	Line	Parenteral	0.05	0.23
Penicillin + Beta-lactamase inhibitors	Amox + Clav	Parenteral	15.17	16.29
	Amox + Clav	Oral	8.67	8.43
	Amp + Sulb	Parenteral	1.90	1.42
	Pipe + Tazo	Parenteral	14.70	9.72
Extended-spectrum penicillins	Amox	Oral	1.10	0.82
	Ampi	Parenteral	1.94	3.22
Beta-lactamase resistant penicillins	Oxa	Parenteral	4.51	4.70
Beta-lactamase sensitive penicillins	Benzil B	Parenteral	1.41	0.50
Polymyxins	Poli B	Parenteral	11.07	15.10
Sulfonamides + Trimetropin	Sulfa + Tri	Oral	5.07	7.13
Intermediate-acting sulfonamides	Sulfa	Oral	2.19	1.15

Caption: Clarithromycin – Clari; Cefepime – Cefe; Ceftriaxone – Ceftr; Cirpofloxacin – Cipro; Ampicillin – Amp; Amphotericin B – Ampho B; Sulfadiazine – Sulfa; Benzylpenicillin Benzathine - Benzyl B; Metronidazole – Metro; Linezolid – Line.
Source: Prepared by the authors.

Among the antimicrobials that showed the greatest percentage variations in the phases of the study, a large consumption of clarithromycin (>50%) was observed at the beginning of phase I, gradually decreasing over the six months analyzed, with the increased use of other antimicrobials (Tables 2a and 2b). The high consumption of benzathine benzylpenicillin and amphotericin B in July 2010 and August 2010, respectively, stands out. The consumption of both antimicrobials decreases drastically in phase II. The beginning of phase II is characterized by greater consumption of cefepime and ceftriaxone (Tables 2a and 2b).

Table 3 describes the frequencies of microorganisms isolated in the two periods, highlighting *Acinetobacter baumannii* in phase I and *Escherichia coli* in phase II.

Table 2a – Monthly consumption of antimicrobials per DDD/1000 patient-days – Phase I.

	Consumption per DDD - Phase I (month/2010)					
Drug	**5**	**6**	**7**	**8**	**9**	**10**
Clari	10.50	11.55	17.22	11.35	14.11	5.51
Cefe	1.87	3.03	2.32	2.73	3.78	5.22
Ceftr	47.93	64.59	50.64	53.31	57.91	42.36
Cipro	1.78	2.48	2.18	1.95	2.69	2.72
Amp	0.79	1.62	2.07	2.11	2.74	2.25
Ampho B	0	0	0.49	5.05	8.64	5.62
Sulfa	3.40	0.96	0.28	3.93	3.92	0.56

Benzyl B	0	0	5.66	0	2.80	0
Metro	0	0.55	1.29	1.02	0.42	1.00
Line	0	0	0.06	0	0.22	0
Total	66.27	84.78	82.21	81.45	97.23	65.24

Caption: Clarithromycin – Clari; Cefepime – Cefe; Ceftriaxone – Ceftr; Cirpofloxacin – Cipro; Ampicillin – Amp; Amphotericin B – Ampho B; Sulfadiazine – Sulfa; Benzylpenicillin Benzathine - Benzyl B; Metronidazole – Metro; Linezolid – Line.
Source: Prepared by the authors.

Table 2b – Monthly consumption of antimicrobials per DDD/1000 patient-days – Phase II.

	Consumption per DDD - Phase II (month/2011)					
Drug	**2**	**3**	**4**	**5**	**6**	**7**
Clari	4.12	7.35	4.68	3.10	6.24	7.12
Cefe	9.72	9.98	4.53	5.43	5.65	6.23
Ceftr	59.50	54.26	53.85	37.38	46.64	41.91
Cipro	3.93	3.68	3.66	3.52	2.33	6.09
Amp	1.26	1.84	2.88	4.06	5.12	4.04
Ampho B	1.84	1.17	1.54	1.71	0.84	3.22
Sulfa	0	1.36	0.50	2.49	1.47	0
Benzyl B	0	0	0	0	0	2.97
Metro	0.90	1.36	1.02	1.13	0.94	0
Line	0	0	0.54	0.84	0	0
Total	81.27	81.00	73.20	59.66	69.23	71.58

Caption: Clarithromycin – Clari; Cefepime – Cefe; Ceftriaxone – Ceftr; Cirpofloxacin – Cipro; Ampicillin – Amp; Amphotericin B – Ampho B; Sulfadiazine – Sulfa; Benzylpenicillin Benzathine - Benzyl B; Metronidazole – Metro; Linezolid – Line.
Source: Prepared by the authors.

Table 3 – Resistant microorganisms among patients who used antimicrobials.

Microorganisms	Phase I N (%)	Phase II N (%)	Total N
Acinetobacter baumannii	92 (23.41)	43 (20.98)	135
Staphylococcus aureus	85 (21.63)	8 (3.90)	93
Pseudomonas aeruginosa	42 (10.69)	20 (9.76)	62
Staphylococcus epidermidis	33 (8.40)	19 (9.27)	52
Staphylococcus haemolyticus	23 (5.85)	6 (2.93)	29
***Klebsiella* sp**	15 (3.82)	7 (3.41)	22
***Enterobacter* sp**	14 (3.56)	5 (2.44)	19
Proteus mirabilis	11 (2.80)	28 (13.66)	39
Staphylococcus hominis	11 (2.80)	4 (1.95)	15
***Enterococcus* sp**	10 (2.54)	16 (7.80)	26
Escherichia coli	8 (2.04)	22 (10.73)	30
Coagulase Negative *staphylococcus sp*	8 (2.04)	3 (1.46)	11
Staphylococcus capitis	5 (1.27)	8 (3.90)	13
***Serratia* sp**	4 (1.02)	1 (0.49)	5
***Staphylococcus* sp**	4 (1.02)	5 (2.44)	9
ESBL-producing *Klebsiella pneumoniae*	3 (0.76)	2 (0.98)	5
Group B *Streptococcus agalactiae* (beta hemolytic)	3 (0.76)	0	3
Non-pneumococcal *Streptococcus* sp (alfa hemolytic)	3 (0.76)	0	3
Alcaligenes faecalis	2 (0.51)	0	2
ESBL-producing *Escherichia coli*	2 (0.51)	1 (0.49)	3
KPC-producing *Klebsiella pneumoniae*	2 (0.51)	2 (0.98)	4
Morganella morganii	2 (0.51)	2 (0.98)	4

Sphingomonas paucimobilis	2 (0.51)	0	2
Streptococcus pyogenes	2 (0.51)	0	2
***Achromobacter* sp**	1 (0.25)	0	1
***Haemophilus* sp**	1 (0.25)	0	1
Providencia stuartii	1 (0.25)	0	1
Salmonella group	1 (0.25)	0	1
Staphylococcus auricularis	1 (0.25)	0	1
Stenotrophomonas maltophilia	1 (0.25)	0	1
Streptococcus pneumoniae	1 (0.25)	0	1
Citrobacter freundii	0	1 (0.49)	1
ESBL-producing *Proteus mirabilis*	0	2 (0.98)	2
Total	**393 (100)**	**205 (100)**	**598**

Source: Prepared by the authors.

In Table 4, it is observed that patients who used antimicrobials in phase I had a greater chance of presenting BR (OR=1.50, 95%IC:1.17 – 1.93), a lower chance of using only one antimicrobial (OR= 0.83, 95%IC:0.72 – 0.95) and greater chance of readmission (OR=1.30, 95%IC: 1.09 – 1.56), compared to phase II patients. The variables BR positivity (OR=1.48, 95%IC: 1.13 – 1.93) and number of hospitalizations (OR=1.27, 95%CI: 1.05 – 1.54) remained in the analysis multivariate (Table 4).

Table 4 – Univariate and multivariate analysis of the variables under study, considering phases I and II.

	Phase I vs Phase II (Univariate)		Fase I vs Fase II (Multivariate)	
	OR	**CI 95%**	**OR**	**CI 95%**
Resistance				
Negative	1		1	
Positive	1.499	1.166-1.927	1.477	1.133 – 1.926
Gender				
Male	1		___	___
Female	1.002	0.896 - 1.121		
Age				
< 50 years	1		___	___
≥ 50 years	1.052	0.944 - 1.171		
Antimicrobial use per patient				
≥4	1		1	
3	1.05	0.878 - 1.255	1.148	0.954 - 1.382
2	0.961	0.811 - 1.139	1.07	0.894 - 1.281
1	0.825	0.715 - 0.951	0.932	0.796 - 1.090
Length of hospital stay				
≤ 7 days	1		___	___
> 7 days	1.007	0.904 - 1.122		
Number of hospitalizations				
1	1		1	
>1	1.304	1.088 - 1.562	1.271	1.051 - 1.538

Source: Prepared by the authors.

DISCUSSION

The results presented initially demonstrate that the profile of patients studied in both periods is similar, with the two populations being potentially comparable. Data regarding the use of antimicrobials during hospitalization demonstrate that the average amount of antimicrobials used in the second phase was slightly lower when compared to the first. However, there is an increase in the average DDD in phase II in relation to phase I.

The DDD refers to the average maintenance dose per day for a drug in its main indication used in adults.[15] The DDD does not necessarily reflect the dose prescribed per day, due to the need for adjustments considering the individual characteristics of each patient. Therefore, DDD-based drug utilization data provides an estimate of drug consumption.

A variation in consumption between phases and an increase in the consumption of broad-spectrum antimicrobials, such as meropenem and linezolid, was observed, despite the identification of a decrease in the frequency of bacteria for which these drugs are frequently indicated to (*Pseudomonas aeruginosa* and *Acinetobacter baumannii*). This may be associated with an increase in the daily dose used. An increase in the consumption of the drug vancomycin was also observed, which contrasts with the decrease in the frequency of microorganisms of the genus *Staphylococcus* sp.

The augmented consumption of strategic antimicrobials may indicate issues related to the empirical use of broad-spectrum antimicrobials in cases of suspected infection with a resistant microorganism before the release of culture results, but it may also be indicative of irrational use of antimicrobials. Furthermore, it is important to highlight that, in practice, these situations are evaluated considering the clinical aspects of the patients and the results of global exams, these being the criteria for defining the therapeutic approach until culture exams are made available.[16] These findings suggest the implementation of interventions that promote the rational use of antimicrobials.

In this context, reducing the consumption of antimicrobials involves rationalizing their use, and if this rationalization does not occur effectively, the simple implementation of the restrictive measure is not enough to guarantee the reduction of both RB and excessive use of antimicrobials. [13] Knowing that the indiscriminate use of antimicrobials is related to the occurrence of RB, the implementation of strategies that prevent irrational use is an action seen as interesting for the study setting.[13]

A reduction in the consumption of drugs recommended for situations with greater complexity of the clinical condition, as amphotericin B and cefotaxime, was observed. The results suggest that patients with less complex infections may have been admitted, and a lower frequency of resistant microorganisms in the second phase. The scientific literature already demonstrates how BR in the community influences BR in the hospital setting.[12] In fact, a study carried out in a hospital suggests that the restrictive measure contributed to a reduction in the incidence of hospital infections.[12,17]

Even with the reduction in RB in the hospital under study after the implementation of the restrictive measure,[12] this is not a strategy that guarantees the rationalization of antimicrobial prescription and, consequently, a reduction in consumption.[18] Factors such as patients' health conditions, proximity between the beds and precarious sanitary measures facilitate the spread of cross-infections by resistant microorganisms, therefore they must be avoided.[7]

It is important to highlight situations such as the antimicrobial linezolid, for which a high variation in general consumption was observed between phases I and II (+390.06), but, in the monthly analysis, consumption was observed in specific months (July and September 2010 and April and May 2011) in phases I and II, respectively. Furthermore, regarding

the frequency of patients who used this antimicrobial in both phases, 2 and 1 patients are observed, respectively. This suggests that the increase in consumption may be associated with a longer period of antimicrobial use or higher doses by patients with specific clinical characteristics. In this sense, analyzes of the indications for the use of antimicrobials and treatment time would allow a more reliable overview of the consumption of antimicrobials.

As positive aspects, a decrease in the occurrence of BR was identified in phase II when compared to phase I. It was also observed that the chance of resistance occurring among individuals who made use of antimicrobials before the restrictive measure was approximately 1.48 (IC95 %:1.13 – 1.93) times higher than those who used antimicrobials after the commercialization restriction. Although the assessment of resistance was not widely addressed in the present study, the literature points to the association of a decrease in hospital BR after the implementation of the restrictive measure.[12]

Another aspect is the identification of the decrease in the average number of antimicrobials used per patient. Despite the decrease in BR after the implementation of the restrictive measure, the increase in consumption of certain antimicrobials could contribute to the subsequent occurrence of resistant microorganisms.

The results obtained are not restricted to a single hospital unit, but encompass different clinics of a teaching hospital, which represents a diverse spectrum of health conditions.

The study contributes to a better knowledge of the use of antimicrobials in the Brazilian reality and points to issues related to the limitation of the restrictive measure for rationalizing the use of antimicrobials. Furthermore, the study points to the need to implement parallel strategies related to qualifying the use of antimicrobials and preventing BR.

Actions to control and reduce infections caused by resistant microorganisms are complex in nature and must include strategies related to the implementation of educational practices for rational prescription, development and implementation of clinical protocols, supervision of prescriptions, hand hygiene campaigns, among others.[18]

The lack of categorization of BR and DDD of antimicrobials according to the type of culture test performed, the impossibility of associating the consumption of each ATB with the occurrence of BR and the impossibility of associating the use of antimicrobials with the duration of treatment are limitations of this study.

It is considered interesting to carry out an analysis of the variation in the consumption of antimicrobials in the institution under study in the long term, as well as the variation in the occurrence of BR.

As a proposal for future studies, this research can be expanded to other contexts to verify whether the results are different and whether there is any good practice involved that can overcome the challenges presented in this conclusion.

CONCLUSION

After the implementation of the restrictive measure on the commercialization of antimicrobials in Brazil, there was an increase in the general consumption of antimicrobials in a defined daily dose within a teaching hospital, with an increase and decrease being identified depending on the class analyzed. Despite the increase in general consumption, it was observed that the variety of antimicrobials prescribed per patient and resistance to microorganisms decreased. It should be noted that this isolated data do not allow a direct association with the restrictive measure, and additional studies are recommended.

RESUMO

Introdução: O consumo de Antimicrobianos (ATB) tem sido descrito como uma das causas da Resistência Bacteriana. Em 2010, foi publicada no Brasil a RDC 44, que restringe a venda gratuita de ATB para reduzir a resistência antimicrobiana em hospitais. **Objetivo:** Identificar o consumo de antimicrobianos antes e após a medida restritiva para comercialização de antimicrobianos no Brasil. **Delineamento:** Estudo transversal realizado em um hospital geral de ensino. Realizou-se análises em duas fases, utilizando as variáveis consumo de antimicrobianos, expresso em dose diária definida e média de uso de diferentes antimicrobianos por paciente e a frequência de micro-organismos resistentes no período, com dados obtidos por meio do prontuário eletrônico. **Resultados**: A média de uso de antimicrobianos diferentes por paciente foi 2,56 (Desvio Padrão (DP) ± 2,02) e 2,40 (DP ± 1,89) nas fases I e II, respectivamente (p=0,0007). A variação geral em dose diária definida foi de 1,89%, porém observou-se medicamentos com variação negativa (claritromicina:-53,32%). A partir do consumo mensal observou-se que a variação geral de linezolida (390,06%) estava em pontos isolados nos dois períodos. Observou-se maior frequência de micro-organismos resistentes isolados na fase I em comparação com a fase II (OR=1,48, IC: 1,13-1,93, respectivamente). **Implicações:** O estudo sugere que existe diferença no consumo de antimicrobianos entre os períodos. Houve aumento no consumo geral de antimicrobianos em dose diária definida, o que pode estar associado ao uso de maiores doses de antimicrobianos. Observou-se menor média de antimicrobianos diferentes por pacientes e menor ocorrência de micro-organismos resistentes.

DESCRITORES

Anti-Infecciosos; Resistência a Medicamentos; Farmacovigilância; Uso de Medicamentos.

RESUMEN

Introducción: El consumo de Antimicrobianos (ATB) ha sido descrito como una de las causas de la Resistencia Bacteriana. En 2010, se publicó en Brasil la RDC 44, que restringe la libre venta de ATB para reducir la resistencia a los antimicrobianos en los hospitales. **Objetivo:** Identificar el consumo de antimicrobianos antes y después de la medida restrictiva para la comercialización de antimicrobianos en Brasil. **Delineación**: Estudio transversal realizado en un hospital general universitario. Los análisis se realizaron en dos fases, utilizando las variables consumo de antimicrobianos, expresado en dosis diaria definida y uso promedio de diferentes antimicrobianos por paciente y frecuencia de microorganismos resistentes en el período, con datos obtenidos a través de la historia clínica electrónica. **Resultados:** El uso promedio de diferentes antimicrobianos por paciente fue de 2,56 (Desviación Estándar (DE) ± 2,02) y 2,40 (DE ± 1,89) en las fases I y II, respectivamente (p=0,0007). La variación general de la dosis diaria definida fue del 1,89%, pero se observaron medicamentos con variación negativa (claritromicina: -53,32%). Del consumo mensual, se observó que la variación general del linezolid (390,06%) fue en puntos aislados en los dos períodos. Se observó una mayor frecuencia de microorganismos resistentes aislados en la fase I en comparación con la fase II (OR=1,48, IC: 1,13-1,93, respectivamente). **Implicaciones:** El estudio sugiere que existe una diferencia en el consumo de antimicrobianos entre períodos. Hubo un aumento en el consumo general de antimicrobianos en una dosis diaria definida, lo que puede estar asociado con el uso de dosis más altas de antimicrobianos. Se observó un menor número promedio de diferentes antimicrobianos por paciente y una menor aparición de microorganismos resistentes.

DESCRIPTORES

Antiinfecciosos; Resistencia a Medicamentos; Farmacovigilancia; Utilización de Medicamentos.

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The data is held at the teaching hospital where the research was carried out and can be accessed by any author of the article.

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CONFLICTS OF INTEREST

There are no conflicts of interest to declare.