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RESTRICTED USE ANTIMICROBIALS AND THEIR USE IN THE MICROBIOLOGICAL CONTEXT IN A PRIVATE HOSPITAL IN SALVADOR

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Abstract: The objective of this study was to identify the consumption of antimicrobials over the years, as well as the relationship of prescriptions in the microbiological profile and in the rates of HAI in the hospital unit. To standardize the calculation, surveillance of consumption of Vancomycin and Teicoplanin was established as restricted for gram positives and Meropenem and Imipenem as restricted for gram negatives. When comparing the prevalence of use of antimicrobials, we found that only in 2009 there was an adequacy of prescription for the identification of microorganisms. All cultures carried out from January 2007 to December 2010 were evaluated and compared year by year. In all years, gram negative agents predominated. HAI rates did not show a statistically significant change over the years. In a second analysis, we found that there was an increase in the prescription of antimicrobials when compared from 2008 to 2007. In the other years, the prescription remained constant. However, the increase in resistance to Vancomycin was progressive. In 2007 the percentage of MRSA was 37.5; followed by 42.1 in 2008; 46.15 in 2009; 64.7 in 2010. After this analysis and considering that in 2007 the percentage of resistance to oxacillin was 37.5%, and 64.7% in 2010, the proposal is to reassess the prescription of first-line antimicrobials at the beginning of treatment. Safe prescribing is the best way to reduce resistance. Further studies will be needed to better understand the impact of medical prescription on antibiotic resistance.
Keywords: Antimicrobials, microbiology, bacterial pharmacoresistance.

INTRODUCTION

Issues related to the prescription of antimicrobials go beyond technical knowledge, often covering emotional and philosophical aspects of the prescriber. The uncertainty regarding the prognosis of the critically ill patient can lead to the empirical prescription of antimicrobials, without the knowledge of the local flora (ANVISA, 2008). There is a constant change in the world microbiological profile. Bacterial resistance to antimicrobials has been shown to be increasingly high to current medications, a fact that leads to a growing concern about the rational use of antimicrobials. The rational use of drugs, according to the WHO, is defined as the administration of appropriate drugs to patients according to their clinical needs, in doses that meet their individual characteristics, at the lowest cost to them and to society (WHO, 2002).). The inappropriate use of antibiotics generates problems not only at the individual level, but also to an entire ecosystem involved in that context (AVORN, SOLOMON, 2000). In recent years, several studies have shown that educational measures for the prescriber of these medications have a positive impact on resistance control. (ROUMIE ET AL., 2005).

Identifying the consumption of antimicrobials in a particular institution, as well as the microbiological profile of the same, is the first step towards an adequate prescription. Conscious prescription is the result of the work of the entire team. Our objective with this work is to identify the consumption of antimicrobials over the years, as well as the impact of prescriptions on the microbiological profile and rates of HAI in the hospital unit. We hope to contribute with this analysis to a reflection on this topic that is of indisputable relevance for the infection controller.

GOALS

- Identify, through medical records and an antibiotic prescription control sheet, the consumption of restricted use antimicrobials in four years;

• Evaluate changes in the Institution's microbiological profile;
• Analyze the rates of Health Care-Related Infection (HAI) over four years and the impact of multidrug-resistant (MR) microorganisms on the absolute number of infections.
• Function as an instrument for the CCIH to promote the surveillance of antimicrobial prescribing.

METHODOLOGY

Retrospective study carried out from the analysis of secondary data produced by the Hospital Infection Control Commission (CCIH) of a private hospital in Salvador, as well as the microbiological profile of the unit verified from the cultures with a sensitivity profile provided by the microbiology laboratory to the CCIH of the institution. Confrontation of this information with the HAI rate, evaluating the impact of MR agents on the absolute number of HAIs.

Phases:

1. Capture of the survey of positive cultures from 2007 to 2010 made by the CCIH;
2. Use of the total number of departures in each year evaluated, to determine the annual prevalence rate of antimicrobial consumption;
3. Evaluation of the microbiological profile of the unit provided to the CCIH by the microbiology laboratory, establishing the prevalence of gram positive and gram negative (with altered sensitivity profile or not);
4. Capture of the restricted use antibiotic prescription survey in the period from 2007 to 2010;
5. Confrontation of the prevalence of gram positive and negative, as well as the sensitivity profile, with the annual consumption rate of restricted use antibiotics;
6. Survey of HAI rates through hospital infection control service reports, verification of HAIs with identified MR etiological agent and finally, determination of the impact of these agents on the total number of HAIs;
7. Discussion of the evidence demonstrated from the verification of the occurrence of an outbreak of a given microorganism, as well as any changes in the microbiological profile that may have occurred.

Ethical aspects

All data used were secondary data previously treated by the institution's CCIH, and individual data were not used for this work. According to demand, information already dealt with and published in hospital reports was requested. There was consent from the hospital management to carry out the present study.

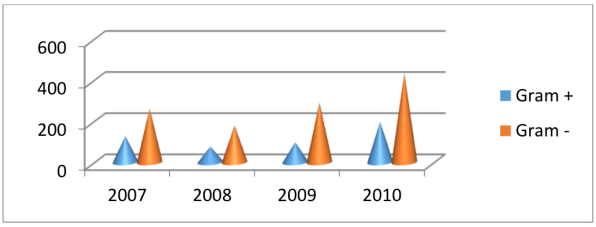
RESULTS

The annual prevalence rate of antimicrobial consumption was determined from the consumption of antibiotics reported by the pharmacy, with the total number of outputs provided by the CCIH in the denominator. Table 1 shows the average length of stay of hospitalized patients in the period from 2007 to 2010. This Table also shows the total number of days of hospitalization and the total number of annual departures from the institution. The mean length of stay provides the mean length of stay for patients. Between 2007 and 2010, the average length of stay varied from 5.18 to 6.86 days per patient.

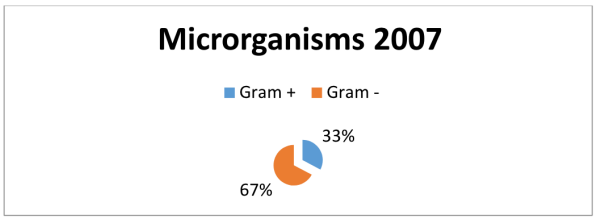
2007	Total of days	Exits	Average Stay
2007	25879	4454	5,81
2008	23986	4630	5,18
2009	27583	4330	6,37
2010	28247	4116	6,86

Table 1: Average Stay from 2007 to 2010.

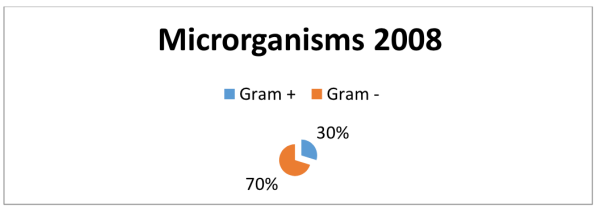
Graphs 1, 2, 3, 4 and 5 demonstrate the annual incidence of microorganisms. In all years there was a predominance of gram negative agents according to the analysis: 2007, 33% gram positive, 67% gram negative; 2008 30% gram positive, 70% gram negative; 2009, 25% gram positive, 75% gram negative; 2010, 31% gram positive, 69% gram negative.



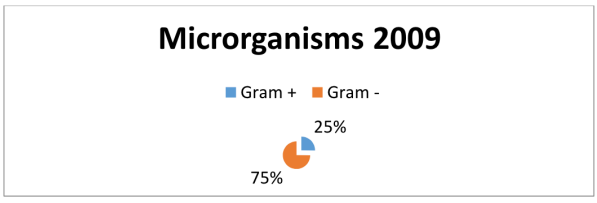
Graph 1: Annual incidence of germs.



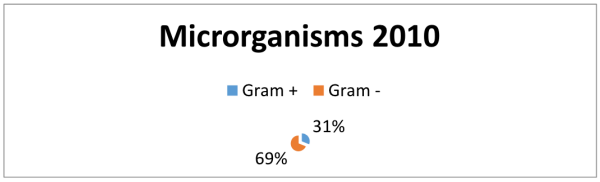
Graph 2: Gram positive vs gram negative incidence of 2007.



Graph 3: Gram positive vs gram negative incidence of 2008.



Graph 4: Gram positive vs gram negative incidence of 2009.



Graph 5: Gram positive vs gram negative incidence of 2010.

As for antimicrobials, we established two groups. The first compound by Vancomycin and Teicoplanin presented the following prevalence, respectively: 2007, 0.92 and 0.11; 2008, 2.4 and 0.76; 2009, 1.96 and 0.85 and 2010, 2.6 and 0.68. The second group composed of Meropenem and Imipenem presented the following prevalence, respectively: 2007, 0.94 and 0.13; 2008: 2.53 and 1.36; 2009, 13.79 and 0.42; 2010, 3.28 and according to Tables 5, Table 6 and Graph 6.

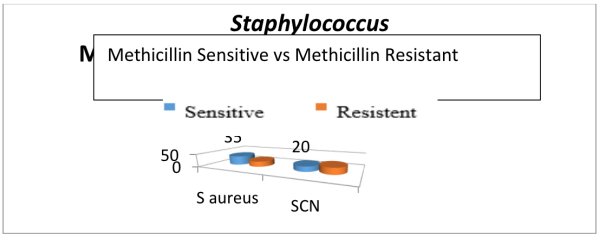
ANTIBIOTIC	2007	2008	2009	2010
Vancomycin	41	111	85	107
Teicoplanin	05	35	37	28
Linezolid	00	00	00	03
Tigecycline	00	00	00	01
Piperacillin/ Tazobactam	94	254	353	249
Meropenem	42	117	164	135
Imipenem	06	63	18	06
Ertapenem	00	00	00	00
Aztreonam	11	31	03	16
polymyxin B	02	04	13	20
Total	201	615	675	565

Table 2: Comparison of the absolute number of patients with restricted use of antimicrobials from 2007 to 2010.

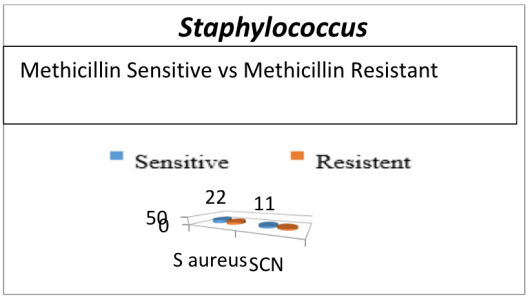
ANTIBIOTICS	2007	2008	2009	2010
vancomycin	0,92	2,4	1,96	2,6
Teicoplanin	0,11	0,76	0,85	0,68
Linezolid	0	0	0	0,07
Tigecycline	0	0	0	0,02
Piperacilina/ Tazobactan	2,11	5,48	8,15	6,04
Meropenem	0,94	2,53	13,79	3,28
Imipenem	0,13	1,36	0,42	0,14
Ertapenem	0	0	0	0
aztreonam	0,25	0,67	0,07	0,39
polymyxin B	0,04	0,09	0,3	0,48
Total	4,51	13,28	15,59	13,73

Table 3: Comparison of the prevalence of consumption of restricted use antimicrobials in the years 2007 to 2010.

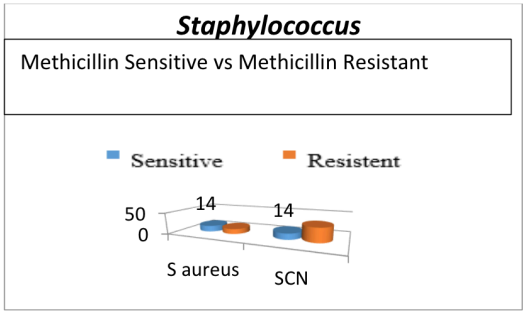
These results show that only in 2009 there was an adequate prescription for this aspect of the microbiological profile. In a second analysis, we found that there was an increase in the prescription of antimicrobials when compared from 2008 to 2007. In the other years, the prescription remained constant. However, the increase in resistance to Vancomycin was progressive. In 2007 the percentage of MRSA was 37.5; followed by 42.1 in 2008; 46.15 in 2009; 64.7 in 2010.



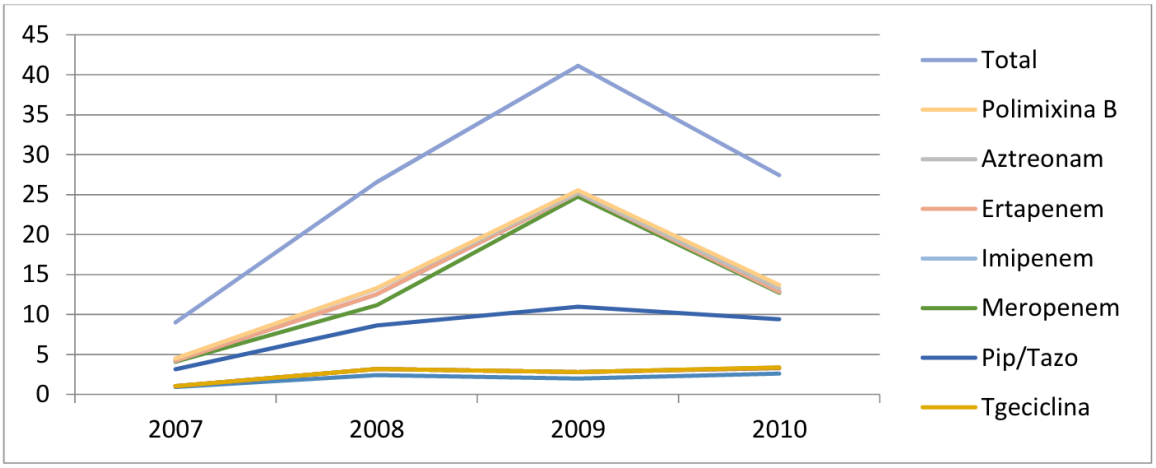
Graph 7: Incidence of *Staphylococcus Methicillin Resistant X Methicillin Resistant 2007.*



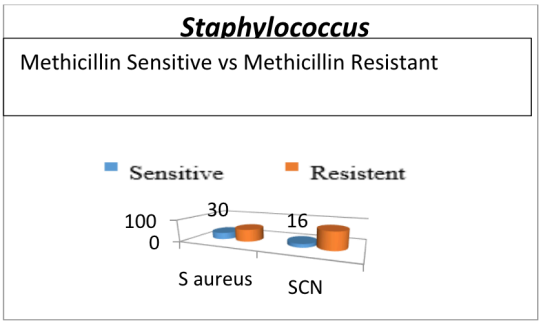
Graph 8:Incidence of *Staphylococcus* Methicillin Resistant X Methicillin Resistant 2008.



Graph 9:Incidence of *Staphylococcus* Methicillin Resistant X Methicillin Resistant 2009.

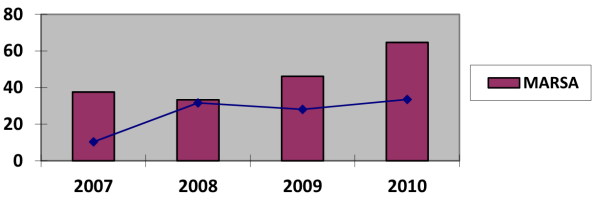


Graph 6: Prevalence of consumption of restricted-use antimicrobials in the years 2007 to 2010.



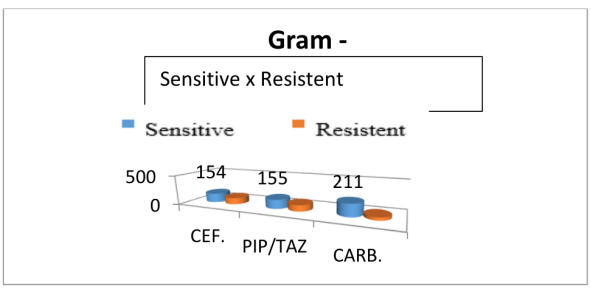
Graph 10: Incidence of Methicillin Resistant X Methicillin Sensitive *Staphylococcus* 2010.

We observed an increase in the consumption of restricted antibiotics between 2007 and 2008 despite a slight decrease in the incidence of S. aureus MRSA. In subsequent years, despite the increase in the identification of this germ in cultures, the increase in antibiotic consumption was not proportional, as shown in Graph 11.



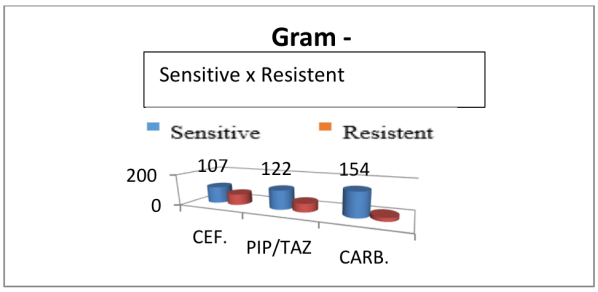
Graph 11: Identification of MRSA X Consumption of Restricted Antimicrobials.

Regarding gram negative germs, we observed that there was a higher incidence of multisensitive gram negative germs in relation to multidrug resistant ones.

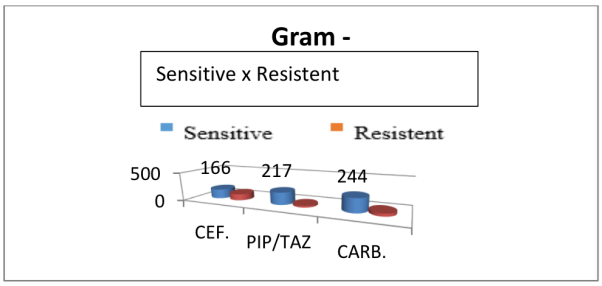


CEF-Cephalosporins; PIP/TAZ-Piperacillin/ Tazobactam; CARB. -Carbapenems.

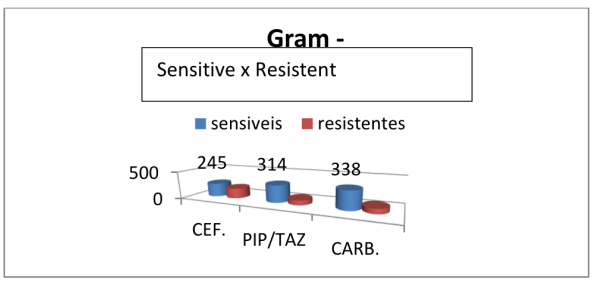
Graph 12: Incidence of gram negative MR X gram negative MS 2007.



Graph 13: Incidence gram negative MR X gram negative MS 2008.

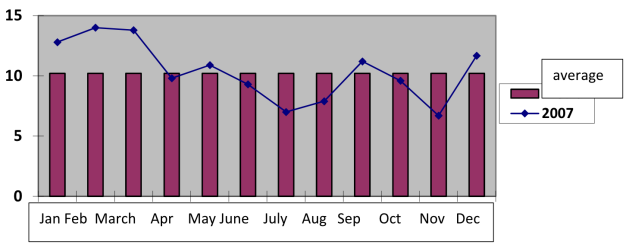


Graph 14: Incidence gram negative MR X gram negative MS 2009.



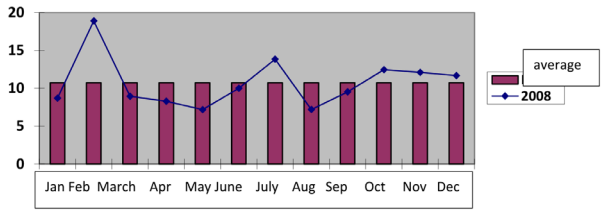
Graph 15: Incidence of gram negative MR X gram negative MS of 2010.

Analyzing the HAI Density, we found that there was a slight increase in 2009, but with a large variance it did not represent a statistically significant increase.



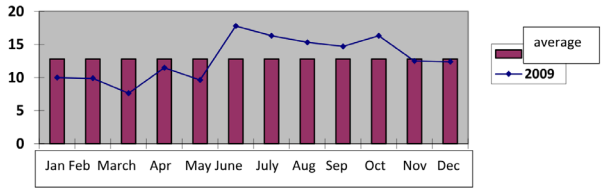
Graph 16: Endemic curve of 2007.

The average HI (Density Rate) for 2007 was 10.2, with a standard deviation of 4.8, considering $p < 0.05$.



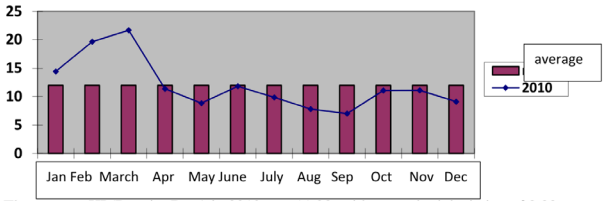
Graph 17: 2008 endemic curve.

The average HI (Density Rate) for 2008 was 10.74, with a standard deviation of 6.53 considering $p < 0.05$.



Graph 18: 2009 endemic curve.

The mean HI was 12.82, considering the density rate for calculations, with a standard deviation of 9.32 with $p< 0.05$.



Graph 19: 2010 endemic curve.

The average HI (Density Rate) in 2010 was 11.98, with a standard deviation of 8.88 considering $p < 0.05$.

DISCUSSION

Currently, the term Health Care-Related Infection is used (IRAS), *healthcare-associated infection,* replacing the term Hospital Infection. This modification has a wider scope, as, in addition to considering infections acquired in the hospital, it encompasses those related to procedures performed in outpatient clinics, day hospitals, home care and infections acquired by health professionals in the work environment (occupational infections). In neonatology, for example, HAIs are divided into late and early, since the infection that occurs in the first 48 hours of life is attributed to Infection acquired as a result of monitoring before birth. (CDC, 2007). Hospital infections are also defined as those manifested before 48 hours of hospitalization, when associated with diagnostic and/or therapeutic procedures performed during this period. Patients from another hospital who are admitted with infection are considered to have a nosocomial infection from the hospital of origin hospital infection (BRAZIL, 1998). Several factors therefore contribute to the occurrence of nosocomial infection. We highlight the irrational use of antimicrobials, the lack of good practices for performing the procedures, the increase in the frequency of invasive procedures and the clinical and immunological conditions of the patient (GADELHA, 1997). The first three causes must be carefully observed in order to prevent this situation. According to the Pan American Health Organization, more than 1.4 million people have complications from nosocomial infections (PAHO, 2005). Brazil does not have accurate information. The underestimation of information would be the cause of this problem, thus, one of the important results of this study would be to sharpen scientific curiosity for the production of data to be used as a tool for the infection controller. Additionally, ordinance 196 of June 24, 1983 of the Ministry of Health instituted the implementation of Hospital Infection Control commissions in all hospitals, public or private, in the country. (BRAZIL, 1983). From this ordinance several commissions were formed, being the ordinance 2616 of 1998 that defined the implementation of the Hospital Infection

Control Program (PCIH). This program is defined as the set of actions developed deliberately and systematically, with a view to the maximum possible reduction in the incidence and severity of nosocomial infections.

It is up to this program to manage antimicrobial resistance (BRASIL, 1998), in this context, we once again ratify the importance of this study as a surveillance strategy for the country's Infection Control Commissions, promoting a surveillance system on the occurrence and transmission of infections, use of antimicrobials and microbial resistance (MARANGONI, VIEIRA, 1998). According to the Pan American Health Organization (PAHO, 2002), in Brazil, in addition to guaranteeing access to health services and quality medicines, it is necessary to implement care practices that promote the rational use of medicines, providing results that directly influence health indicators. The WHO draws attention to the inappropriate use of antimicrobials, especially for non-bacterial infections or in incorrect doses. It also describes the excessive use of injectable formulations and self-medication (WHO, 2002). Data from the CDC indicate that 50 million of the annual prescriptions of antimicrobials carried out in outpatient clinics in the United States are considered unnecessary. Very commonly, antimicrobials are prescribed to treat colds and other viruses. (CDC 2005). Other authors point to inadequate surgical prophylaxis (HEINECK et al, 1999; HEINECK et al, 2002) and to the empirical use and prescription of antibiotics for fever of undefined cause (MOREIRA, 2004). The participation of the pharmaceutical industry through advertising for the dissemination of its products can influence the medical prescription, so it is necessary to maintain a critical view at the time of prescription (AVORN; SOLOMON, 2000). The rational and responsible prescription depends on the updating and modification of behavior by prescribers (STEIN et al., 2004). There is, for example, a significant increase in the use of fluoroquinolones with a consequent increase in bacterial resistance (McDOUGALL et al., 2005; LINDER, et al., 2005). In the United States, (LAUTHENBACH et al., 2003) observed that 81% of Fluoroquinolone prescriptions were inadequate. Furthermore, when the prescription was considered to be clinically correct, in only one case the dose and duration of treatment were adequate. Another aspect to be observed refers to bacterial resistance, which despite being considered a natural biological phenomenon, must be treated as a public health problem. The emergence of bacterial strains resistant to each introduction of a new antimicrobial agent is verified (WHO, 2001). The emergence of multidrug-resistant bacteria, which multiply even at higher antimicrobial concentrations than those considered therapeutic, is a reality. Infectious processes by these bacteria can quickly lead to the death of hospitalized patients. (WANNMACHER, 2004). Ten years after the discovery of Penicillin, even before its release for clinical use, the presence of beta-lactamases had already been identified, thus characterizing resistance of some species (MOREIRA, 2004). Acquired resistance occurs due to continued exposure to antimicrobial agents, resulting in the development of new defense mechanisms generated by mutations in the genetic material of the bacterium (FUCHS, 2004). Excessive use of antimicrobials leads to selective pressure, promoting the selection of multiresistant germs, these microorganisms remain as colonizers of patients and part of the environmental microbiota - which in turn will be agents of subsequent infections (ANVISA).

Measures such as the implementation of policies for rational use and monitoring

of the use of antimicrobials, updating of professionals, surveillance of the increase in resistance and creation of the pharmacy and therapeutics commission (WHO, 2000), this way, we highlight the surveillance strategy as the main result. of this job. Aiming to associate the existence of microorganisms resistant to the consumption of antimicrobials, DANCER and collaborators (2006), carried out a study in a university hospital for a period of 04 months and concluded that patients who were hospitalized in Units with higher consumption of antimicrobials had infections by germs. multidrug resistant more often. This same resistance profile was also found in the environment (surfaces) of each unit, in addition to the employees' hands (DANCER et al., 2006). Another study carried out in intensive care units (ICU) in France showed that, after the implementation of protocols for the use of antimicrobials, there was a decrease from 37% to 15% in the rates of nosocomial infections caused by multidrug-resistant germs. These protocols guided the empirical use with subsequent adjustment in therapy after the antibiogram result. It also established the need to justify the prolongation of antibiotic therapy time. The use of oral fluoroquinolones was encouraged for the lowest cost. There was also a decrease in the association of aminoglycosides, aiming to reduce possible adverse effects and toxicity (GEISSLER et al., 2003). In China, between 1996 and 2002, an epidemiological surveillance program was implemented to monitor the susceptibility of gram negative bacteria. The researchers found that the percentage of multidrug resistant Pseudomonas aeruginosa strains increased from 11.5% to 20.5% between 1996 and 2006. The authors pointed to the need for programs to control bacterial resistance in hospitals. They also guided the implementation of manuals that can guide the prescription and use of antimicrobials, especially in empirical therapy (WANG; CHEN, 2005). Another study carried out in Spain between 1986 and 2002, with the objective of analyzing the resistance of S. aureus, found increased rates of resistance. For Oxacillin from 1.5% to 31%, Erythromycin from 7% to 31.7%, Ciprofloxacin from 0.6% to 33.9% and Clindamycin that showed no resistance in 1986 to 20.1% in 2002 (CUEVAS et al., 2004). Evaluating the present study, considering that in 2007 the percentage of resistance to oxacillin was 37.5%, would a prescription with first-line antimicrobials have had an impact on the 64.7% in 2010? Further studies will be useful for further clarification. Here, attention is also paid to the need for continuing education, demonstration of the microbiological profile and training of professionals for a safe prescription. All these data confirm that bacterial resistance is a global problem (WHO, 2001). Thus, controlling the use of antibiotics and regulating their prescription are fundamental for the control of bacterial resistance.

CONCLUSION

In a detailed retrospective analysis of secondary data from the CCIH, the consumption of antimicrobials classified as restricted over four years of follow-up was identified. To standardize the calculation, surveillance of consumption of Vancomycin and Teicoplanin was established as restricted for gram positives and Meropenem and Imipenem as restricted for gram negatives. When comparing the prevalence of use of antimicrobials, we found that only in 2009 there was adequacy of prescription for identification of microorganisms. All cultures carried out from January 2007 to December 2010 were evaluated and compared year by year in order to verify changes in the microbiological profile, observing gram positive and gram negative germs as shown in graph 17. gram negative agents. The HAI

rates were also evaluated and compared with the microbiological profile and the prescription of antimicrobials, with no statistically significant change in rates over the years. In a second analysis, we found that there was an increase in the prescription of antimicrobials when compared from 2008 to 2007. In the other years, the prescription remained constant. However, the increase in resistance to Vancomycin was progressive. In 2007 the percentage of MRSA was 37.5; followed by 42.1 in 2008; 46.15 in 2009; 64.7 in 2010. Would the prescription of drugs with a lower spectrum of action have an impact on the pattern of oxacillin resistance? Further studies will be useful for further clarification. The surveillance strategy, if used systematically, will provide data for infection control and the formulation of new strategies to control resistance. Safe prescribing is the best way to reduce resistance. Further studies will be needed to better understand the medical prescription in antibiotic resistance, as well as to formulate effective antimicrobial policies.

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