Epidemiological aspects of the occurrence of Vancomycin-resistant *Enterococci*

ASPECTOS EPIDEMIOLÓGICOS DA OCORRÊNCIA DO ENTEROCOCCUS RESISTENTE A VANCOMICINA

ASPECTOS EPIDEMIOLÓGICOS DE LA EVENTUAL APARICIÓN DEL *ENTEROCOCCUS* RESISTENTE A LA VANCOMICINA

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ABSTRACT

This descriptive study was conducted in a public hospital from May 2005 to October 2007, with the purpose to determine the epidemiological aspects that involve vancomycin-resistant enterococci (VRE) and describe the evolution of patients. |The data was obtained from registers on patient records and then processed in SPSS. Frequency distribution and measures of central tendency were used. A total 122 patients participated of the study, the majority were males with an average age of 43 years (SD= 18.8), and 16.3% developed VRE infection. Vancomycin has been the most used antibiotic (62,3%), 97.5% used invasive procedures, 45.0% were dependent on intensive care nursing, 77.9% had at least one open wound and 50.8% progressed to death. The data suggests that recommendations for bacterial resistance control should be encouraged to reduce mortality, morbidity, hospital costs and thus provide better quality care to patients.

KEY WORDS

Infection.
Cross infection.
Risk factors.
Drug resistance, bacterial.

RESUMO

Estudo descritivo realizado em um hospital público, de maio de 2005 a outubro de 2007. Objetivou-se determinar os aspectos epidemiológicos que envolvem o Enterococcus resistente à vancomicina (VRE) e descrever a evolução dos pacientes. Os dados foram coletados de registros em prontuários. Após a coleta, as informações foram processadas no SPSS. Usou-se a distribuição de frequência e medidas de tendência central. Participaram do estudo 122 pacientes. A maioria foi do sexo masculino, com idade média de 43 anos (DP= 18,8). A infecção por VRE foi desenvolvida por 16,3%. O antimicrobiano mais usado previamente à identificação do VRE foi a vancomicina (62,3%); 97,5% foram submetidos aos procedimentos invasivos; 45,0% eram dependentes de cuidados intensivos de enfermagem; 77,9% tinham pelo menos uma ferida aberta, e 50,8% evoluíram a óbito. Esses dados sugerem que recomendações de controle da resistência bacteriana devem ser encorajadas diuturnamente, visando à redução da mortalidade, morbidade, custos hospitalares e, consequentemente, uma melhor qualidade da assistência ao paciente.

DESCRITORES

Infecção.
Infecção hospitalar.
Fatores de risco.
Farmacorresistência bacteriana

RESUMEN

Estudio descriptivo, realizado en un hospital público desde mayo de 2005 a octubre de 2007. Se objetivó determinar los aspectos epidemiológicos que involucran al Enterococcus resistente a vancomicina (VRE) y describir la evolución de los pacientes. Los datos fueron recolectados de registros en historias clínicas, después de la recolección, la información obtenida fue procesada en SPSS. Se usó la distribución de frecuencia y medidas de tendencia central. Participaron del estudio 122 pacientes. La mayoría, de sexo masculino, con edad media de 43 años (DP = 18,8). El 16,3% desarrolló infección por VRE. El antibiótico más usado antes de la identificación del VRE fue la vancomicina. (62,3%); 93,5% fueron sometidos a procedimientos invasivos, 45,0% dependían de cuidado intensivo de enfermería, 77,9% tenía por lo menos una herida abierta y 50,8% fallecieron. Tales datos sugieren que deben ser alentadas en forma ilimitada medidas de control de la resistencia bacteriana, apuntando a la reducción de la mortalidad, morbilidad, costos hospitalarios y, consecuentemente, a una mejor calidad de atención del paciente.

DESCRIPTORES

Infección.
Infección hospitalaria.
Factores de riesgo.
Farmacorresistencia bacteriana.

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INTRODUCTION

Hospital infections are currently considered a public health issue affecting more than 15% of hospital patients. Moreover, the problem may be worsened in case there is bacterial resistance [1]. In the last few decades, more and more multiple drug-resistent bacteria have been identified, and *Enterococcus* stands out among them.

Vancomycin-resistant *Enterococcus* (VRE) was first identified in Europe in 1986, and then spread out throughout other countries. In the USA, a 28.5% rate is estimated for VRE in intensive care therapy units. In Latin America, VRE prevalence increase is found in Argentina, Uruguay and Chile[2-4].

In Brazil, the first reports of VRE appeared in Curitiba (1996), then in São Paulo and Rio de Janeiro[5]. In Minas Gerais, its first appearance in health units was in 2005; however, there are no reports on the subject until today.

Despite the availability of guidelines on control and prevention measures for VRE in health units, rates are growing and raise concerns among the multiprofessional team[2,4,6].

The presence of Vancomycin-resistant *Enterococcus* presents social and economic implications. Treatments of vancomycin-resistant *Enterococcus* are estimated to be ten times more expensive than *Enterococcus* infection. Moreover, it is associated to a significant mortality increase[7-8].

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In addition to care costs, patients and family members' experiences related to VRE also stand out due to the risk of acquiring a hospital infection that is difficult to treat, isolation and visiting restrictions. Another aspect regards the need for health professionals to prevent contamination (using gloves and gowns), in addition to financial costs with Individual Protection Equipment (IPEs), can be understood by patients and family members as more severe.

OBJECTIVE

Due to the relevance of the theme, this study has the aim to describe epidemiological aspects that involve the colonization and dissemination of VRE and describe the evolution of patients.

METHOD

This is a descriptive epidemiological study of a quantitative approach performed in a large public hospital involved with research education, and part of the network of facilities of the State of Minas Gerais Hospital Foundation – FHEMIG in Brazilian acronyms. The institution has 273 beds and it is a state reference in specialized urgency and emergency care for automobile accidents trauma, melee and fire weapon abuses, burns, drowning, falls, intoxications and clinical situations that involve imminent death risks.

It represents an average of 8,750 monthly emergency appointments, 710 hospital admittances/month and 353 surgeries/month. The institution counts on 1,617 professionals: 578 physicians, 126 nurses, 854 nursing technicians and assistants, 42 physiotherapists, and 20 social workers.

The target population consisted of patients admitted to the hospital, carriers of vancomycin-resistant *Enterococcus*. Initial identification of the VRE carrier was done as from the vigilance culture of critical patients performed weekly by perianal and nasal swabs, as the Infection Control Commission routine in the Hospital. The measure has the aim to detect early cases and search for the reduction of resistant microorganisms' dissemination, both in hospital environment and in the community.

Carriers were understood as those who presented one or more positive VRE cultures, despite the material or colonized or infected situation.

The definition of colonization was translated into the condition where there was a growth and multiplication of the microorganism in the organism's epithelial surfaces, without causing a specific immunological response, disease or infection[8]. On the other hand, the infection regarded the condition in which there was a tissue reaction resulting from the invasion, multiplication or action of a toxin produced by infectious agents in the host organism[8].

In order to include participants in this study, the following criteria were considered: a) patient admitted to the Institution, regardless of the unit, with vancomycin-resistant *Enterococcus* verified by a microbiologic exam performed as from May 2005 until the end of data collection on October 30th of 2007; b) available data in the medical files, in the Hospital Infection Control Service charts and registration in the microbiology laboratory.

Patients were evaluated according to the following variables: Gender, age, origin, time of hospital stay (before and after VRE identification), patients' dependency degree according to nursing care, open wounds, invasive procedures use, anti-microbes use in days, death, and infected or colonized by VRE.

In order to classify patients' dependency degree for the Patients Classification System (PCS), food intake, mobilization, hygiene, awareness level, eliminations, medications, and special procedures parameters were used. The use of PCS in evaluating risk factors in vancomycin-resistant *Enterococcus* colonization or infection is based on the presumption that more dependant patients are also more manipulated, which increases the contamination risk by resistant microorganisms through the hands of health professionals[8].

In order to analyze patients' dependency degree, this variable categorization was performed according to COFEN (Federal Council of Nursing Practice) Resolution 189/1996[9]. The following parameters were defined: a) Minimum care: provided to stable patients under the clinical and nursing point of view, physically self-sufficient regarding basic human needs; b) Intermediate care: provided to stable patients, under the clinical and nursing point of view, requiring medical and nursing evaluations partially dependant on nursing professionals for basic human needs; c) Semi-intensive care: provided to recoverable patients, under no eminent death risk, susceptible to vital functions instability, requiring permanent and specialized nursing and medical care; d) Intensive Care: provided to severe and recoverable patients, with imminent death risk, susceptible to vital functions instability, requiring permanent and specialized medical and nursing care.

The statistical analysis was performed by using the *Statistical Package for Social Sciences* (SPSS), version 13.0, 2004, initially based on the sample characterization. In this stage, frequency tables beyond the use of central tendency measures (mean, median, standard deviation) were used for quantitative variables and frequencies distribution for qualitative variables.

The evaluation and approval of the Research Ethics Committee of the institution and the Research Ethics Committee of the Federal University of Minas Gerais preceded this study, under REC No.061/07, according to Resolution 196 of 1996 of the National Council of Health that regulates researches in human beings.

Considering that data were collected from medical files and Hospital Infection Control Service data base, and when consent forms were not available due to hospital release, transfer or death of the patient, the authorization to access files was obtained from hospital directors.

RESULTS

This study included 122 carriers of vancomycin-resistant *Enterococcus* during the period of May, 2005 through October, 2007. Figure 1 presents the distribution of the absolute number of patients identified as VRE carriers and the number of samples identified according to the month and year.

During this study, an exponential increase in positive cultures of VRE going form 17 cases in 2005 to 57 cases in 2006 was observed. And, until October of 2007, 48 cases were identified.

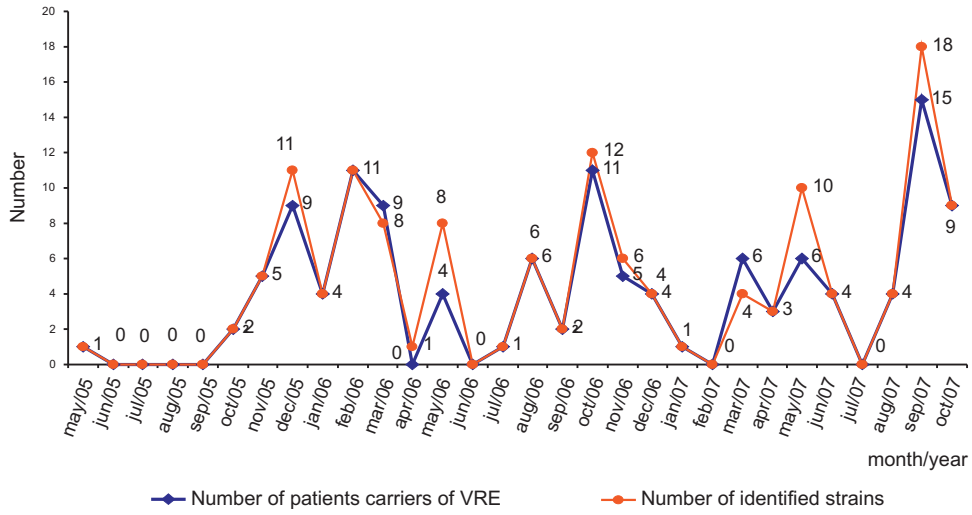

Figure 1 - Distribution of VRE carriers (n=122) and number of vancomycin-resistant *Enterococcus* samples (n=135) according to the month and the year of identification - Belo Horizonte - 2007

Socio-demographic characteristics of vancomycin-resistant Enterococcus *carriers*

A predominance of 83.6% (102) of VRE carriers was observed, most likely due to the high number of trauma victims (a reference of the hospital in this study) are males (Table 1).

Regarding patients' age, there was a variation between 1 and 90 years, mean of 43 (SD=18.8) and median of 41 years. (Table 1).

The percentage of outside patients - those who did not report having come from other health institutions - was of 56.6% (69), where most were trauma victims, followed by 35.2% (43) coming from their residence and 8.2% (10) were transferred from other institutions (Table 1).

All patients were admitted to the Intensive Care Units (ICU) and the Progressive Care Unit (PCU), most probably due to its similarity to the intensive therapy. The PCU is mostly constituted by patients who require intensive/semi-intensive or intermediate care, where more than 60% of patients need mechanical ventilation and/or presented some type of sequel from the base disease, and it is considered a long stay unit.

Table 1 - Distribution of Patients in this study according to demographic variables - Belo Horizonte - May of 2005 to October of 2007

Demographic Variables	# of patients	%
Sex		
Male	102	83.6
Female	20	16.4
Age		
≤ 13 years	4	3.3
14 - 26 years	29	23.8
27 - 39 years	30	24.8
40 - 52 years	29	23.8
53 - 65 years	18	14.8
≥ 66 years	12	9.9
Origin		
Residence	43	33.8
Outside	69	57.5
Other health institution	10	8.7

Regarding hospital stay previous to VRE identification among VRE carriers, there was a variation from five to 892 days, with mean of 55.4 (SD=86.0) and median of 41 days.

Hospital Stay time is considered a significant factor in the acquisition of resistant microorganisms. In this present study, 8.3% of patients were identified with VRE within less than five days of hospital stay, reaching 18% within fifteen days of hospital stay (Figure 2).

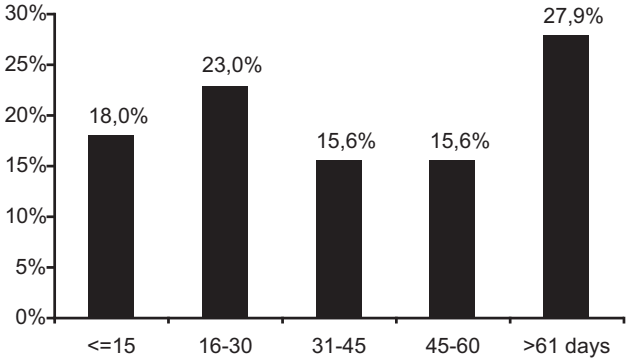

Figure 2 - Distribution of patients in the study according to hospital stay previous to VRE - Belo Horizonte - May of 2005 to October of 2007

Regarding hospital stay in intensive care units, from all 122 patients in this study, 82.8% (101) were previously in the unit with a mean of 25.6 days (SD=37.9) and median of 19.5 days.

Regarding patients' degree of dependence on the nursing team, patients who were classified as dependent on intensive nursing care were observed in 45% (55) of the cases. Clinical and more severe surgery patients who needed monitoring and continuous life support, carriers of disease and clinical conditions that generally predispose VRE colonization and infections were found in this category (Figure 3).

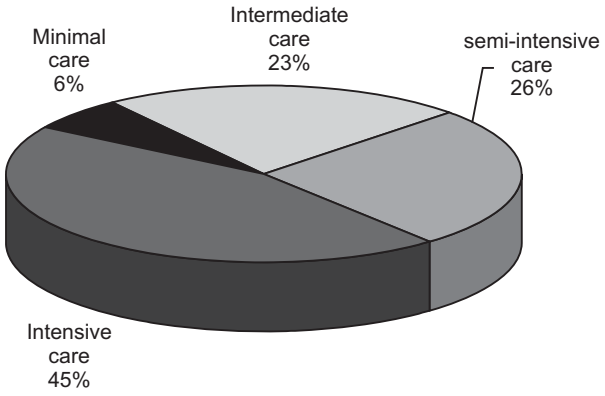

Figure 3 - Distribution of patients according to the dependency degree regarding nursing care - Belo Horizonte - May of 2005 to October of 2007

The fact that 23.0% (28) of patients need intermediate care, 26.3% (32) semi-intensive care and only 5.7% (7) minimum nursing care, stands out.

Most VRE carriers in this study, 77.9% (95), had at least one open wound. Lying ulcers in those patients corresponded to 68.0% (83) of the open wound cases, 44.6% (37) demonstrated more than one injured site. The sacral region was common in patients with pressure ulcer.

Invasive procedures among patients in this study were verified in 97.5% (119). Among procedures, indwelling catheter was present in 97.0% (119) of VRE carriers, followed by mechanical ventilation in 92.6% (115).

The mean of anti-microorganisms use previously to VRE was of eleven days (SD=14), with median of ten. Among anti-microorganisms agents there are the vancomycin with 62.3% (mean of 19 days, SD=14.2), fourth generation cephalosporin with 50.8% (mean of 11.3 days, SD=7.4), third-generation cephalosporin with 45.9% (mean of 11.3 days, SD= 7.0), quinolones with 40.2% (mean of 11.3 days, SD=5.73), and carbapenems with 32.8% (mean of 14.5, SD= 8.1).

Isolated VRE microbiologic profile and infections caused by VRE

Among all 122 carriers of VRE, 135 vancomycin-resistant *Enterococcus* strains were isolated, and eight patients were colonized by two different species of *Enterococcus.* Five species of VRE were found: E. *faecalis* (76), E. *faecium* (39), E. *gallinarium* (6), E. *avium* (6), E. *casseiliflavus* (1). And no specimen was identified in seven isolated *Enterococcus*.

Among all patients in this study, 22 (18.04%) developed hospital infection by VRE and 81.96% colonization. Despite the isolation of five species of VRE, only E. *faecalis* (63.6%) and E. *faecium* (31.8%) were related to infection. In patients characterized with VRE infection, the most frequent site was the urinary system, corresponding to 72.8% (16) followed by blood stream infection, with 9.9% (2), soft tissue infection with 9.0% (2), respiratory system with 4.5% (1), and surgery infection 4.5% (1).

Clinical evolution of VRE carriers

The mean of hospital stay for patients after the identification of VRE was of 48 days (SD=62.9), median of 28.5 and standard deviation of 63 days. Regarding patients' evolution, 50.8% (62) of cases evolved to death, 34.4% (42) were released from the hospital and 4.9% were transferred to another health institution. At the end of data collection in October 30th , 9.8% (12) patients were still in the hospital.

From the 62 patients who evolved to death, only 6.5% (4) demonstrated evidence that allowed for relating them to the presence of vancomycin-resistant *Enterococcus,* since those patients, at the time of death, were infected by the microorganism.

DISCUSSION

The increase of patients colonized by VRE constitutes a worldwide problem[10]. A study involving European, Latin American and North American countries, in the period of 1998 to 2004, found growth in the number of patients with vancomycin-resistant *Enterococcus*, presenting rates twice higher in seven years in North America, of 8.6% in 1998 to 14.8% in 2004.

In Europe, the growth was less expressive until 2003, and in 2004, there was a growth of 6.3% in relation to the previous year[11]. In Brazil, the idea about VRE epidemiology situation is still not accurate.

Hospital stay is widely known as a risk factor for acquiring VRE and, in ICU cases beyond seven days, it was demonstrated as a risk factor for acquiring VRE, ($p< 0.05$)[11-12]. Despite the well-known relation between hospital stay and the acquisition of VRE, in this present study, a statistically significant association between those two variables was not possibly established.

Another aspect related to hospital stay - although not evaluated in this present study, but important – is the fact that it can work as a transferring facilitating factor for VRE through health professionals' hands. Hands can be contaminated with VRE by the use of objects or through patients' skin, intact surfaces and the transfer of those organisms to other surfaces that can be confirmed by cultures, isolated molecular typing, and follow up on the adherence of prevention protocols and infection control. Therefore, hospital stay can still mean a higher possibility of horizontal transmission caused by professional-patient, professional-environment and infected patient-environment contacts[11].

Parting from that, the importance of the dependency degree of the patient in relation to the nursing staff consisting the quantitative/qualitative care level classification required by the health institution where the client stands, must be pointed out[9].

Although it regards the analysis of the dependency degree on the nursing team, it also indirectly expresses the need for the evaluation and manipulation of the patient regarding the whole multiprofessional team.

Therefore, it means that more severe patients are more manipulated, needing more health professional care, whether by higher adherence to individual protection equipments, which are important in cases of microorganisms-resistant carriers (glove and gown), above all in the care for hand washing before and after the contact with these and all other patients and /or still in performing procedures.

Moreover, the data observed regarding patients' dependency degree on nursing care point out the role those professionals represent in the control and prevention of resistant microorganisms inside the health institution, contributing specifically for the nursing staff as parameter for personnel calculations and in care planning [9,13].

Studies demonstrate that the contact with patients colonized by VRE favors health professionals' infections, as well as the contact with infected surfaces in wards where vancomycin-resistant *Enterococcus c*arriers are found. The number of procedures performed is also associated to VRE acquisition by professionals. Although the type of care regarding VRE colonization is not evaluated, studies support that colonized patients contact is a risk factor for the dissemination of this condition in health units, mainly among patients and professionals[11,14].

Regarding the use of anti-microorganisms, it is pointed in literature as an important factor for the development of *vancomycin-resistant Enterococcus*. A study carried out in 2001 demonstrated that VRE prevalence was strongly associated to the use of vancomycin and that in a linear regression model, vancomycin ($p< 0.001$) and

third-generation cephalosporin ($p=0.02$) were independently associated to VRE prevalence[12].

According to literature, the frequency of isolated species can vary according to the population in the study. A study involving 49 laboratories in 27 European countries found the predominance of E. *faecium.* In Turkey and Latvia, one third of VRE were E. *casseiliflavus* and two thirds were E. *Gallinarium*[15].

Analysis in VRE prevalence in kidney transplant patients found a frequency of 50% of E. *faecium* and E. *faecalis* and 28.9% of E. *Gallinarium*[16].

CONCLUSION

Regarding epidemiological aspects involving VRE occurrence, positive cultures exponential increase from 17 cases in 2005 to 57 in 2006 was demonstrated. Until October of 2007, 48 cases were identified.

Most patients with VRE were males with average age of 43 years (SD=18.8) and victims of some type of trauma. Hospital stay in intensive care units and progressive care units were predominant, corresponding to patients with higher morbidity and longer stays.

Among VRE carriers, only *E. faecalis* and *E. faecium* were related to infections.

Vancomycin was the more used anti-microorganism previously to the identification of VRE. Most patients in this study used invasive procedures and almost half of them were dependent on nursing intensive care.

Regarding evolution, half of the patients in this study evolved to death and VRE association was low (6.5%).

In conclusion, the importance of disclosing rates of resistant microorganisms' epidemiological profile in many hospital units is evident. A careful care for prevention and control measures on bacterial resistance is needed and, above all, for VRE dissemination with the commitment of all professionals involved in the care.

Moreover, a permanent educational program, monitoring measures as hand washing, active culture surveillance (hospital stay, weekly and high risk patients' cultures) and consequently isolation of positive VRE patients. In addition to cases studies and disclosure of results on strategies adopted and their impact in clinical practice through open clinical and/or theme seminars meetings to all members of the multiprofessional team.

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