ORIGINAL ARTICLE

Risk factors associated with the acquisition of multiresistant bacteria in a pediatric nursery

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Abstract

Objective: to identify the risk factors in the patients with multiresistant bacteria during their stay in a pediatric Intensive Care Unit and in a pediatric nursery of a tertiary teaching hospital.

Method: review of records of patients who stayed in these units from January 1995 to July 1997, and who had a multiresistant microorganism (infection or colonization) isolated. Case-control study used the McNemar test for group comparison and stepwise logistic regression to select independent risk factors. The following risk factors were tested: prior hospital stay, underlying disease, Intensive Care Unit admission, surgical procedure, urinary catheter, central venous line, ventilator, prior antibiotic therapy and skin lesion.

Results: sixty-six multiresistant bacteria (33 gram-negative bacilli and 33 methicillin-resistant *S. aureus)* were identified in 52 patients. The logistic regression analysis of the case-control study identified two risk factors: prior antibiotic therapy and skin lesion. A single risk factor was indicated for patients with gram-negative bacilli. For patients with methicillin-resistant *S. aureus*, central venous line and skin lesion were significant factors.

Conclusion: prior antibiotic therapy and skin lesion were the factors associated with the acquisition of multiresistant bacteria. Skin lesion and central venous line were risk factors for patients colonized by methicillin-resistant *S. aureus*. The strategies to limit the spread of these bacteria in hospitals should take these three factors into consideration.

J Pediatr (Rio J) 2000; 76(4): 275-80: risk factors, multiresistant bacteria, nosocomial infections, methicillin-resistant *S. aureus*.

Introduction

Multiresistant bacteria (MRB) have very often been found in hospitals in the last decades. These bacteria may be transmitted from hospital to hospital by staff or patient carriers. Quarantine for patients coming from another hospital has been suggested as a solution, but has proven impracticable. The application of MRB control measures depends on the knowledge of the bacteria's epidemiology, which is different for multiresistant gram-negative bacteria (MRGNB) and methicillin-resistant *S. aureus* (MRSA). The latter are cross transmitted between patients, healthcare workers, and, sometimes, hospitals.[1-5] MRGNB usually come from the endogenous flora itself, and colonization in adults is closely associated with the use of antimicrobial drugs.[6-12] MRGNB carriers are thus a reservoir of these bacteria, and cross transmission mediated by the hands of healthcare workers may occur.[13]

The identification of these bacteria may also lead to the empiric use of expensive broad-spectrum last generation antibiotics, which generates even more resistance.

The objective of this study is to identify the risk factors for MRB acquisition in children and to contribute to the knowledge of these bacteria's epidemiology.

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Patients and methods

We reviewed the medical records of patients with one or more MRB who were hospitalized in the Pediatric Nursery and the Pediatric Intensive Care Unit, Hospital de Clínicas, Universidade Estadual de Campinas, from January 1995 to June 1997.

The Nursery and the Pediatric Unit have 48 and 10 beds, respectively, for patients with clinical or surgical problems. Thirty percent of these patients come from the Emergency Room. Cancer/oncology patients are not hospitalized in these units. Monthly hospitalization average is 180 patients.

Data about the patient's identification, the bacteria isolated and the site where they were isolated were retrieved from the Nosocomial Infection Control Committee database and from the patients' records. MRB were defined by the Nosocomial Infection Control Committee as methicillin-resistant *S. aureus* and gram-negative microorganisms resistant to aminoglycosides or third-generation cephalosporins.

The Nosocomial Infection Control Committee routinely carries out a weekly survey of MRB in the patients hospitalized for more than 1 week. As soon as bacteria are identified, the Committee advises about contact precautions, and the patient is moved to a single room.

We used the paired case-control methodology to identify risk factors. Control pairing was determined by date of admission (3-day coincidence) and by the patients' ages. Our computer data service provided us with a list of the patients hospitalized on each of the dates when MRB were isolated for each case. The control case was chosen from that list according to the following criteria: a patient who was the same age or the closest age, who was hospitalized at least 3 coinciding days prior to MRB isolation, and who was not infected or colonized by MRB.

The factors surveyed were: previous hospitalizations, diagnosis of underlying disease (we considered all those diagnoses that led to repeated hospitalizations or frequent outpatient service visits, such as chronic renal disease, genetic syndrome, biliary tract atresia, hydrocephalus, chronic respiratory disease, acquired immunodeficiency syndrome, cardiopathies, Hirschprung's disease, etc.), Intensive Care Unit hospitalization, surgical procedure, urinary catheter, central venous line, ventilator, present use of antibiotics (as the study was retrospective, outpatient use was not considered because medical records might have been unreliable), and the presence of skin lesions (trauma lesions, drains, surgical wound and peritoneal dialysis catheter). These factors were only included in the study if present before the detection of MRB.

Patients with cystic fibrosis whose flora was already known at the outpatient service were excluded from the study as this type of flora does not pose any problem to the definition of precautions to be taken when these patients are hospitalized. Patients for whom coagulase-negative *Staphylococcus* was identified were also excluded because of the difficulty to define multiresistance in these cases.

Statistical analysis was carried out with the software SPSS for Windows (SPSS Inc.). Each risk factor was analyzed separately, using the McNemar test for group comparison and considering significance level P<0,05. Multivariate analysis employed traditional logistic regression and conditional logistic regression; the method used was the odds ratio forward analysis.

The present study was approved by the Research Ethics Committee at Faculdade de Ciências Médicas, Universidade Estadual de Campinas.

Results

We identified 66 MRB in 52 patients (Table 1). MRGNB were identified in 30 patients, and MRSA, in 28; in six patients, both groups of bacteria were identified.

The sites of isolation of the bacteria are presented in Table 2. In two of these sites, two MRB were identified. The cases of isolation in the respiratory tract, the skin, and the ocular secretion were classified as colonization, and the other cases were classified as infections.

Table 1 - Multiresistant bacteria isolated in patients hospitalized in Pediatric Nursery and Pediatric Intensive Care Unit from January 1995 to June 1997

Microorganism	Number	Percentage
S. aureus	33	50.0
A. baumannii	10	15.2
P. aeruginosa	8	12.1
E. cloacae	7	10.6
Klebsiella sp	4	6.1
Alcaligenes faecalis	2	3.0
E. aerogenes	1	1.5
Serratia sp	1	1.5
Total	**66**	**100.0**

Average hospitalization time up to first isolation was 14.2 days, and median was 10 days. The antibiotics taken by the patients before the acquisition of MRB were: aminoglycosides (27), cephazolin or cephalexin (18), trimethoprim/sulfamethoxazole (12), third-generation cephalosporin (12), vancomycin (6), chloramphenicol (6), clindamycin (6), ampicillin (5), methicillin (4), others (4).

Table 2 - Isolation site of multiresistant bacteria in patients hospitalized in the Pediatric Nursery and Pediatric Intensive Care Unit from January 1995 to June 1997

Isolation site	Number	Percentage
Central venous line	19	29.7
Respiratory tract	12	18.8
Blood stream	10	15.6
Skin	7	10.9
Surgical wound	6	9.4
Ascitic fluid	4	6.3
Urine	4	6.3
Abscess	1	1.6
Ocular secretion	1	1.6
Total	**64**	**100.0**

The results of statistical analysis of risk factors for patients hospitalized in the Intensive Care Unit before the identification of the multiresistant microorganisms did not differ significantly from the results for patients in the Nursery. Therefore, data for these two groups were analyzed together, as a single group.

Table 3 presents the results for the case-control study. Hospitalization time up to first MRB isolation was not different from the hospitalization times for controls (P=0.60). The occurrence of nosocomial infection was expectedly higher among the study cases than among controls (P<0.001). McNemar test analysis showed that, from the possible risk factors, only the use of antibiotics, central venous line, and skin lesion were significant.

The separate analysis for patients with MRSA presented the same results: use of antibiotics (P=0.001), central venous line (P<0.001), and skin lesion (P=0.002). For patients with MRGNB, only the use of antibiotics (P=0.02) and skin lesion (P=0.0006) were significant.

The Nosocomial Infection Control Committee weekly colonization survey was carried out only for 52% of the cases and 18% of the controls.

The significant variables in the conditional logistic regression were the same found in the traditional logistic regression, which showed that there was no association between the risk factors and the variables used for pairing. Odds ratio for these variables was estimated by traditional logistic regression. The significant variables in the McNemar test were entered in the regression first, and all the other variables were entered after that.

Table 3 - Case-control study: result of McNemar test analysis

	Case	Control	Significance
Number	52	52	
Age (months)			
Average	66.3	61.1	
Median	30.2	26.1	
Number of deaths	6	6	NS*
ICU hospitalization	33	26	NS*
Surgery	16	12	NS*
Previously healthy	17	25	NS*
Chronic disease	33	26	NS*
Outpatient treatment	25	22	NS*
Previous hospitalization	17	19	NS*
Previous hospitalization – another hospital	13	7	
Use of antibiotics	17	9	P<0.001
Urinary catheter	14	13	NS*
Ventilator	24	21	NS*
Central venous line	43	24	P<0.001
Skin lesion	1	15	P<0.001
NI occurrence	38	7	P<0.001

*Not significant

Table 4 -   Results of logistic regression analysis of case-control study

	No. of pairs	Variables	Odds ratio	CI*90%	Significance
All cases	52	Skin lesion	1.99	1.35-2.95	0.0035
		Antibiotics	2.13	1.35-3.36	0.0063
		CVL†	1.59	1.07-2.35	0.0514
Patients with MRSA	28	Skin lesion	2.28	1.19-4.38	0.0375
		Antibiotics	2.20	1.11-4.36	0.0565
		CVL†	2.73	1.41-5.28	0.0121
Patients with MRGNB	30	Skin lesion	1.83	1.19-3.02	0.0248
		Antibiotics	1.93	1.10-3.38	0.0530
		CVL†	—	—	0.7254

* confidence interval   † central venous line

Previous use of antibiotics and skin lesion were significant for the whole group; central venous line and skin lesion were significant for the patients with MRSA; only skin lesion was significant for the patients with MRGNB (Table 4).

Discussion

MRB may cause colonization or infection in hospitalized patients, and it is important to identify the carrier to avoid spread in the hospital. D'Agata et al. studied colonization during a nonoutbreak period and concluded that clinical cultures detect ceftazidime-resistant gram-negative bacilli in only 5% of the total cases detected by colonization surveys.[14] Colonization surveys are justifiable not only to provide adequate care to the patient carrier and guide the empiric antibiotic therapy, but also to try to identify the factors that may be associated with such colonization. Studies carried out in pediatric Intensive Care Units concluded that 10% of the patients are already colonized with MRGNB on the first 3 hospitalization days, and that half of them are already colonized at admission.[15,16]

The results of the present study do not concur with other findings reported in the literature,[6-10,12,14] which list central venous line and prior antibiotic therapy as risk factors for the acquisition of MRB. Multivariate analysis showed that central venous line was a significant risk factor for patients with MRSA.

This effect is not clear in the group analysis of the cases, as the use of central venous line did not prove to be a risk factor for the acquisition of MRGNB. Although the use of antibiotics is considered a risk factor, some authors suggest that the microorganism's and the patient's intrinsic factors may also play a significant role.[17] A study of colonization in a pediatric Intensive Care Unit during a nonoutbreak period showed that the restriction to the use of ceftazidime alone did not reduce the reservoirs of MRGNB,[18] which were also associated with factors external to the hospital, such as treatment in outpatient services for chronic patients. In this study, the use of antibiotics was considered a risk factor for the whole group, but not for the MRSA or MRGNB group of carriers separately, in which cases it showed borderline significance. The fall to borderline significance levels, which are similar for the MRSA and MRGNB groups, is a probable effect of the reduced number of cases in these groups. These findings may reflect the fact that a small number of patients made use of third-generation cephalosporin, which is knowingly associated with the emergence of resistance in gram-negative bacteria.[19,20,21]

Intensive Care Unit hospitalization is considered a risk factor for the acquisition of MRB[12,16] because of the higher frequency of invasive procedures, which promote colonization as they break the natural protective barriers and require more handling. Intensive Care Unit hospitalization was not a significant risk factor for the patients in this study. No significant differences were found for patients in the Nursery and in the Intensive Care Unit. This can be partially explained by the fact that the semi-intensive care beds are all in the Nursery, and almost all patients in those beds have come from the Intensive Care Unit. There is a significant flow of patients between these two units. For the same reason, the admission diagnoses for

patients in the two units are similar. The fact that coagulase-negative *Staphylococcus* were not identified may also have influenced these results, since these bacteria are frequently associated with infections acquired in Intensive Care Units.

The large number of different diagnoses at admission made it impossible to draw an association between the patient's own risk factors, such as primary or secondary immunosuppression and the isolation of MRB. Our results may have been different if the population studied were composed of immunosuppressed patients, especially because these patients usually make frequent use of antibiotics and undergo invasive procedures.

In our analysis, patients with chronic diseases or previous hospitalizations were not more likely to have MRB, which differs from what is reported in the literature.[3,12,14,16,22]

These findings may be explained by the selection of the control group. If controls had been selected differently – that is, for example, patients carrying the same non-multiresistant bacteria, or bacteria identified in the same site –, results might have been different. This type of pairing, however, would have been impossible in a retrospective study. We should also mention that the colonization survey, as programmed, was not carried out for the cases or the controls. Consequently, there might have been colonized patients in both groups that were not identified.

A relevant finding was the strong association of skin lesion with the presence of either gram-negative or gram-positive MRB. Although we found differences between the risk factors for the acquisition of MRGNB and MRSA, the multivariate analysis showed that skin lesion was significant in both groups. The results suggest that this risk factor should be included in colonization surveys.

We concluded that, if the characteristics of the population assisted in our hospital do not change, the survey of multiresistant microorganisms should target patients according to the risk factor they present, and not according to the unit where they are hospitalized, or their diagnosis at admission. As a preventive measure in everyday practice, the use of antibiotics, central venous line and skin lesions should determine the strategies to limit the spread of both gram-positive and gram-negative bacteria in the hospital.

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