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Frequência e perfil de suscetibilidade aos carbapenêmicos de bastonetes Gram-negativos não fermentadores de glicose isolados de amostras clínicas entre 2007 e 2012

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ABSTRACT

Introduction: One of the major problems in health services is the occurrence of healthcare-associated infections (HAIs) by microorganisms resistant to various antimicrobials. **Objectives:** To describe the frequency and susceptibility profile of *Pseudomonas aeruginosa* and *Acinetobacter baumannii* to carbapenems in the hospital from Fundação Santa Casa de Franca, São Paulo, Brazil. **Methods:** The susceptibility of *P. aeruginosa* and *A. baumannii* to carbapenems from 304 clinical isolates between 2007 and 2012 was retrospectively analyzed from a microbiology database at the clinical laboratory of the hospital of Fundação Santa Casa de Franca, São Paulo, Brazil. **Results:** From isolated and identified strains, 236 (5.3%) *P. aeruginosa* were susceptible to imipenem (2007 – 69.6% to 2012 – 41.7%) and meropenem (2007 – 63.3% to 2012 – 25%). In addition, all 68 (1.7%) *A. baumannii* isolates were susceptible to both antibiotics. **Conclusion:** *A. baumannii* resistance to carbapenems was not identified; however, there was a decrease in susceptibility to carbapenems over the years for *P. aeruginosa*.

Key words: carbapenems; microbial drug resistance; *Pseudomonas aeruginosa*; *Acinetobacter baumannii*.

INTRODUCTION

One of the major problems in health services is the occurrence of healthcare-associated infections (HAIs) by microorganisms resistant to various antimicrobials. In hospital settings, non-fermenting Gram-negative bacilli, such as *Pseudomonas aeruginosa* and *Actinobacter baumannii*, stand out as emerging etiological agents of pneumonia and sepsis, with critical patients' mortality of 27%-48%[1-3].

In this context, carbapenems represent one of the therapeutic options for infections against non-fermenting Gram-negative bacilli, although they decrease susceptibility[4-6] and exhibit a relative stability against most extended-spectrum beta-lactamases(ESBL)[7]. For this reason, carbapenems are frequently used as a last resort in the treatment of nosocomial infections caused by Gram-negative bacteria resistant to other beta-lactams or antibacterials[2-4, 8].

The exponential growth of bacterial resistance has demanded monitoring the results of cultures in clinical samples towards the quantitative understanding of antibiotic resistance evolution and the conduction of therapeutic interventions[9].

Thus, the objective of this research was to evaluate the frequency and the susceptibility profile of non-fermenting Gram-negative bacilli (*P. aeruginosa* and *A. baumannii*) to carbapenems.

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METHODS

This is a retrospective observational study conducted on a database at the microbiology sector in the clinical laboratory of the hospital of Fundação Santa Casa de Franca, São Paulo, Brazil. The study covered the period 2007-2012, yielding a total of 4,464 culture results. The project was approved by the Human Research Ethics Committee (CAAE: 22484714.6.0000.5393).

Non-fermenting Gram-negative bacilli (*P. aeruginosa* and *A. baumannii*) were identified by Gram stain and the NF II kit (Probac do Brasil, São Paulo, Brazil), which, according to the manufacturer, encompasses oxidase tests, capacity of growth on MacConkey agar, use of glucose, maltose and lactose into oxidation-fermentation (OF) base medium, lysine and arginine decarboxylation (Moeller base) and gelatin liquefaction.

Antibiogram was done by disc-diffusion method in Petri plates with Mueller Hinton Agar and incubation at 37°C during 24 h, according to current guidelines for selection criteria and cut-off points used for antibiotics – Clinical and Laboratory Standards Institute (CLSI)[10].

For data analysis, descriptive statistics was used in absolute and relative frequency.

RESULTS

Among the 4,464 culture results distributed in the years 2007 (865), 2008 (981), 2009 (485), 2010 (539), 2011 (704) and 2012 (890), 236 (5.3%) strains of *P. aeruginosa* and 68 (1.5%) of *A. baumannii* were isolated.

According to the **Table**, among the isolated and identified strains, 236 (5.3%) *P. aeruginosa* demonstrated greater susceptibility to imipenem (2007 – 69.6% to 2012 – 41.7%) than to meropenem (2007 – 63.3% to 2012 – 25%). However, decreased profiles of susceptibility to carbapenems were revealed over the years. Besides, the 68 (1.7%) *A. baumannii* isolates were susceptible to both antibiotics.

TABLE – Distribution of *Pseudomonas aeruginosa* susceptibility profile to carbapenems (imipenem and meropenem) at a tertiary hospital in Franca (SP), Brazil, from 2007 to 2012

Year	Susceptibility			
	Imipenem		Meropenem	
	n	%	*n*	%
2007	55	69.6	50	63.3
2008	30	62.5	27	56.3
2009	12	60	10	50
2010	14	56	11	44
2011	24	46	22	42.3
2012	5	41.7	3	25
Total	140	59.3	123	52.1

DISCUSSION

In this research, non-fermenting Gram-negative bacilli were more susceptible to carbapenems than those reported by Somily *et al.* (2012)[11], which demonstrated susceptibility to imipenem and meropenem of 9.5% for *A. baumannii* and 9.1% and 18.2%, respectively, for *P. aeruginosa*. Other works[3, 8, 12] presented different frequencies of susceptibility of *A. baumannii* to carbapenems (32.6%, 69.9% and 59%).

Another study, carried out at a tertiary Brazilian hospital, from 1999 to 2008, identified a 3.7-fold increase in the isolation frequency of multidrug-resistant Gram-negative bacilli ($p < 0.001$). *A. baumannii* was the most prevalent bacterium (36.2%), with a 4.8-fold increase ($p < 0.001$), mostly isolated at intensive care units (ICU), ranging from 0% to 62.5%. On the other hand, regarding the multidrug resistance of *P. aeruginosa*, there was an increase of 23.4% to 64.6%[13].

In the south of Brazil, a research at a small hospital, between 2007 and 2009, identified a high frequency of multidrug resistance and genetic diversity. Rates of resistance to carbapenems were observed in 25% of the *P. aeruginosa* isolates and in 50% of *Acinetobacter* spp.[14].

Conversely, out of the 158 *A. baumannii* isolates from 11 hospitals in New York, 31% were susceptible to meropenem (2013-2014), an increase in comparison with the 13% observed in 2009 ($p < 0.0001$). Nevertheless, 481 isolates of *P. aeruginosa* showed increased frequency of susceptibility to meropenem: 79% (2013-2014), when in comparison with the 59% in 2009 ($p < 0.0001$)[15].

Data about hospitals in Latin America from 2002 to 2013 demonstrated rates of resistance to carbapenems of up to 66% and 90% for *P. aeruginosa* and *A. baumannii*, respectively; frequencies higher than 50% were reported in several countries[16].

A possible etiology for the increased occurrence of carbapenem-resistant *P. aeruginosa* and *A. baumannii* in Latin America is patient-to-patient transmission, which is also responsible for local outbreaks and nosocomial dissemination.

The permanence of infections by these microorganisms leads to the use of broad-spectrum antibiotics, especially carbapenems, and increase selective pressure for resistance to these drugs. The presence of *A. baumannii* coincided with the growing use of this class of antimicrobial. Although there is no consensus, the use of antibiotics can be an independent risk factor for the development of *P. aeruginosa* and *A. baumannii* resistance to carbapenems[13, 17-19].

In this study, from 2007 to 2012, the analysis of microbiological culture results allowed concluding that *P. aeruginosa*, identified in 5.3%, was more susceptible to imipenem (69.6% in 2007 to 41.7% in 2012) than to meropenem, but there was a more accentuated decline of susceptibility to meropenem over the years (63.3% to 25%) – Table. *A. baumannii* presented susceptibility to carbapenems, with no alterations in the studied period.

Principally in hospitals, identification of microorganisms with epidemiologic value is globally recognized in terms of antibiotic susceptibility profile. Clinical complications, mortality and the elevated cost associated with infections caused by these etiologic agents reinforce the real necessity for the implementation of a program of active microbiological surveillance in health-care institutions. So, it is essential that health professionals and citizens become more and more aware and involved in the fight against HAIs, above all against increasingly recurrent multidrug-resistant microorganisms.

RESUMO

Introdução: *Um dos grandes problemas nos serviços de saúde é a ocorrência de infecções relacionadas com assistência à saúde (IRAS) por microrganismos resistentes a vários antimicrobianos.* ***Objetivos:*** *Descrever a frequência e o perfil de suscetibilidade de* Pseudomonas aeruginosa *e* Acinetobacter baumannii *aos carbapenêmicos no hospital da Fundação Santa Casa de Franca, São Paulo, Brasil.* ***Métodos:*** *Retrospectivamente, a suscetibilidade de* P. aeruginosa *e* A. baumannii *aos carbapenêmicos foi analisada em 304 isolados clínicos entre 2007 e 2012, a partir de um banco de dados do setor de microbiologia do laboratório clínico do hospital da Fundação Santa Casa de Franca, São Paulo, Brasil.* ***Resultados:*** *Das cepas isoladas e identificadas, 236 (5,3%)* P. aeruginosa *eram suscetíveis a imipenem (2007 – 69,6% a 2012 – 41,7%) e meropenem (2007 – 63,3% a 2012 – 25%). Além disso, todos os 68 (1,7%) isolados de* A. baumannii *eram suscetíveis aos dois antibióticos.* ***Conclusão:*** *Não foi identificada resistência de* A. baumannii *aos carbapenêmicos, no entanto houve diminuição da suscetibilidade aos carbapenêmicos no decorrer dos anos para* P. aeruginosa.

Unitermos: *carbapenêmicos; resistência microbiana a medicamentos;* Pseudomonas aeruginosa*;* Acinetobacter baumannii.

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