



Em tempos de resistência aos carbapenems, é ainda possível reduzir as taxas de resistência antimicrobiana por meio da utilização de programas de racionalização de antimicrobianos?

NÃO

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Conflitos de interesses

(últimos 2 anos)

(S=speaker; R=research; G=grants)

Teva (S), Novartis (SRG), Pfizer (S),
Wieth (S), Bayer (S), MSD (SRG), Astellas
(SR), AstraZeneca (S), Sanofi (S)

Arthur Schopenhauer

*Como Vencer
um Debate
sem Precisar
Ter Razão*

EM 38 ESTRATAGEMAS

(Dialética Erística)

Introdução, Notas e Comentários

Olavo de Carvalho



TOPBOOKS





SUPPLEMENT ARTICLE

Antimicrobial Stewardship: Importance for Patient and Public Health

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Você prescreveu polimixina B sem indicação?



- Baseando-se na evidência:

Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: Guidelines for the Prevention of Antimicrobial Resistance in Hospitals

David M. Shlaes, Dale N. Gerding, Joseph F. John, Jr., William A. Craig, Donald L. Bornstein, Robert A. Duncan, Mark R. Eckman, William E. Farrer, William H. Greene, Victor Lorian, Stuart Levy, John E. McGowan, Jr., Sindy M. Paul, Joel Ruskin, Fred C. Tenover, and Chatrchai Watanakunakorn

From Wyeth-Ayerst Research (Dr. Shlaes), Pearl River, New York; Veterans' Affairs Lakeside Medical Center (Dr. Gerding), Chicago, Illinois; UMDNJ-Robert Wood Johnson Medical School (Dr. John), New Brunswick, New Jersey; William S. Middleton Memorial Veterans' Hospital (Dr. Craig), Madison, Wisconsin; SUNY Health Science Center (Dr. Bornstein), Syracuse, New York; Lahey Clinic (Dr. Duncan), Burlington, Massachusetts; Duluth Clinic Limited (Dr. Eckman), Duluth, Minnesota; St. Elizabeth Hospital (Dr. Farrer), Elizabeth, New Jersey; University Hospital (Dr. Greene), State University of New York, Stony Brook, New York; Bronx-Lebanon Hospital Center (Dr. Lorian), Bronx, New York; Tufts University School of Medicine (Dr. Levy), Boston, Massachusetts; Grady Memorial Hospital (Dr. McGowan), Atlanta, Georgia; New Jersey Department of Health (Dr. Paul), Trenton, New Jersey; Kaiser Permanente Medical Center (Dr. Ruskin), Los Angeles, California; Centers for Disease Control and Prevention (Dr. Tenover), Atlanta, Georgia; and St. Elizabeth Hospital Medical Center (Dr. Watanakunakorn), Youngstown, Ohio

- Como posso dizer que não funciona?



- Minha desculpa:

Clinical Infectious Diseases 1997;25:584–99

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1058–4838/97/2503–000

The Role of Antimicrobial Stewardship to Prevent Spread

- ESCMID 201

ESCMID PUBLICATIONS

ESCMID guidelines for measures to reduce transmission of bacteria in hospitalized

E. Tacconelli¹, M. A. Cataldo², S. J. Danz³,
J. Rodríguez-Baño^{10,11,12}, N. Singh¹³, M. ...

Numerous papers have demonstrated that previous antimicrobial drug exposure is a strong risk factor for colonization and infection due to drug-resistant bacteria [219–222]. Fluoroquinolones and third-generation cephalosporins have often been implicated in promoting the spread of MDR-bacteria [220–222], although, the direct association between antibiotic therapy and the acquisition of antibiotic-resistant bacteria is still unclear. The studies are often confounded by scarce data on antibiotic usage and differ according to microorganism, dosage, drug combinations, timing of exposure and setting. A recent Cochrane systematic review showed that interventions to reduce excessive antibiotic prescribing to hospital inpatients can reduce antimicrobial resistance or hospital-acquired infections and interventions to increase effective prescribing can improve clinical outcome [223].

One of the earlier illustrations of the efficacy of antibiotic intervention is the work by Gerding *et al.* who, to address high rates of gentamicin resistance among GNB, substituted amikacin for gentamicin in the hospital formulary at two

decreased usage of carbapenems was correlated with decreased CRPA and CRAB [226].

Interesting studies on the impact of an ABS programme on antimicrobial resistance were those performed to reduce the morbidity of *C. difficile* diarrhoea. In a study by Malani *et al.* [227] in which there was a review of 510 antimicrobial orders, implementation of an ABS programme was associated with a 50% reduction in the likelihood of developing *C. difficile* infection, and with a 25.4% drop in defined daily doses of the target antimicrobials. There is also increasing evidence to suggest that appropriate antibiotic use can decrease the incidence of MDR-GNB [228,229], even though data are controversial [230].

There are different approaches to the control and limiting of antibiotics consumption in hospitalized patients. Antibiotic restriction, i.e. the requirement for approval of the antibiotic from an infectious diseases specialist might be one of the most effective control methods [231,232]. A variety of such use-justification approaches have been designed to improve antibiotic use. These have included telephone approval from an infectious diseases specialist, automatic stop orders, and antibiotic order forms that require justification for the prescribed drug after dispensing from the pharmacy. At the Indiana University Medical Center a prior approval programme resulted in decreased



[Intervention Review]

Interventions to improve antibiotic prescribing practices for hospital inpatients

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Editorial group: Cochrane

Publication status and date: Edited (no change to conclusions), published in Issue 5, 2013.

Review content assessed as up-to-date: 3 February 2009.

Citation: Davey P, Brown E, Charani E, Fenelon L, Gould IM, Holmes A, Ramsay CR, Wiffen PJ, Wilcox M. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database of Systematic Reviews* 2013, Issue 4. Art. No.: CD003543.

Artigo mais recente é de 2003

Antes de 2009



- Não há recomendações sobre PRA para redução de resistência neste grupo de bactérias

Microorganism					Microorganism					Microorganism				
MDR- <i>K. pneumoniae</i>					MDR- <i>A. baumannii</i>					MDR- <i>P. aeruginosa</i>				
Intervention	Quality of studies [ref.]			Overall quality of evidence	Intervention	Quality of studies			Overall quality of evidence	Intervention	Quality of studies			Overall quality of evidence
	Moderate	Low	Very low			Moderate	Low	Very low			Moderate	Low	Very low	
Hand hygiene	2 [122, 265]	–	–	Moderate	Hand hygiene	4 [81, 122, 153, 157]	1 [274]	–	Moderate	Hand hygiene	2 [122, 275]	1 [274]	–	Moderate
Education	1 [122]	–	–	Moderate	Education	4 [81, 122, 153, 157]	1 [274]	–	Moderate	Education	1 [122]	1 [274]	–	Moderate
Contact precautions	2 [122, 265]	–	–	Moderate	Contact precautions	4 [81, 122, 153, 157]	–	–	Moderate	Contact precautions	1 [122]	–	–	Moderate
Isolation room	1 [265]	–	–	Moderate	Isolation room	1 [81]	–	–	Moderate	Isolation room	–	–	–	Insufficient
Environmental cleaning	2 [122, 265]	–	–	Moderate	Environmental cleaning	4 [81, 122, 153, 157]	–	–	Moderate	Environmental cleaning	1 [122]	–	–	Moderate
Antimicrobial stewardship	1 [268]	1 [269]	–	Moderate	Antimicrobial stewardship	1 [268]	2 [269, 272]	–	Moderate	Antimicrobial stewardship	2 [268, 275]	2 [269, 272]	–	Moderate



Crit Care Med. 2006 Feb;34(2):329-36.

Comparison of antimicrobial cycling and mixing strategies in two medical intensive care units.

Martínez JA¹, Nicolás JM, Marco F, Horcajada JP, García-Segarra G, Trilla A, Codina C, Torres A, Mensa J.

- Rodízio vs. *mixing* (cada paciente usa uma classe diferente)
 - Não compara com um controle

Am J Infect Control. 2009 Apr;37(3):204-9. doi: 10.1016/j.ajic.2008.06.008. Epub 2008 Nov 4.

The effect of limiting antimicrobial therapy duration on antimicrobial resistance in the critical care setting.

Marra AR¹, de Almeida SM, Correa L, Silva M Jr, Martino MD, Silva CV, Cal RG, Edmond MB, dos Santos OF.

- Redução do tempo de antibiótico
 - Mostrou redução de resistência de carbapenêmico em *Klebsiella* e *Pseudomonas*



[Eur J Clin Microbiol Infect Dis](#). 2010 Aug;29(8):1015-24. doi: 10.1007/s10096-010-0964-5. Epub 2010 Jun 4.

Rotation of antimicrobial therapy in the intensive care unit: impact on incidence of ventilator-associated pneumonia caused by antibiotic-resistant Gram-negative bacteria.

[Raineri E¹](#), [Crema L](#), [Dal Zoppo S](#), [Acquarolo A](#), [Pan A](#), [Carnevale G](#), [Albertario F](#), [Candiani A](#).

No difference in ICU mortality and crude in-hospital mortality between T1 and T2 was noted. Moreover, no significant change of microbial flora isolated through clinical cultures was observed. We were able to conclude that, despite global microbial flora not being affected by such a programme, antibiotic therapy rotation may reduce the incidence of VAP caused by antibiotic-resistant Gram-negative bacteria in the ICU, such as *Pseudomonas aeruginosa*. The application of this programme may also improve antibiotic susceptibility. However, further studies are needed to confirm our results.

[Infect Control Hosp Epidemiol](#). 2011 Jun;32(6):584-90. doi: 10.1086/660100.

Hand hygiene, and not ertapenem use, contributed to reduction of carbapenem-resistant *Pseudomonas aeruginosa* rates.

[Pires dos Santos R¹](#), [Jacoby T](#), [Pires Machado D](#), [Lisboa T](#), [Gastal SL](#), [Nagel FM](#), [Kuplich NM](#), [Konkewicz L](#), [Gorniak Lovatto C](#), [Pires MR](#), [Goldani LZ](#).

- Alguma dúvida?



Por que faltam evidências?

imipenem (18% per year) and gentamicin (12% per year) compared with the pre-intervention trend. Significant changes in the rates of gentamicin and ciprofloxacin susceptibility were also observed in the inducible Enterobacteriaceae group, although these were less clinically significant [243].

One of the major issues when planning an intervention to reduce inappropriate usage of antibiotics within healthcare facilities is that clinical studies have often been limited by selection biases, small sample sizes, limitation to single institutions, inadequate pre-observation and post-observation datum points, and failure to deal with confounders. As pointed out by McGowan and Tenover, studies that demonstrate improved susceptibilities following a reduction in antibiotic use should be confirmed through multicentre prospective trials that adjust for common confounding factors, especially heightened IPC efforts and biases [244].

The aforementioned strategies can be incorporated into comprehensive programmes, designed to optimize antimicrobial therapy, to improve patient outcomes, ensure cost-effective therapy and reduce the adverse effects associated with antimicrobial use, including antimicrobial resistance. However, a few studies included in their outcomes the evaluation of the impact of an ABS programme on the resistance rate levels. When ABS is implemented in response to the emergence of resistance in a facility, in a multifaceted intervention, it is difficult to determine exactly what resulted in the decrease in the emergence of resistance.



Assunto novo?

Talvez não falte só evidência....
... Mas falte experiência... (tempo)



Quem tem bactéria MDR? - ESBL

**Não é possível atribuir o risco
de MDR apenas em
antibióticos**





Quem tem bactéria MDR? - ESBL

Revista da Sociedade Brasileira de Medicina Tropical 43(4):452-454, jul-ago, 2010



Communication/Comunicação

Epidemiology of extended spectrum β -lactamase producing *Enterobacter* bacteremia in a Brazilian hospital

Duration of hospitalization	61.2 \pm 81.3	27.7 \pm 23.6		< 0.05
Risk factor - n (%)				
intensive care unit	20 (71.0)	13 (43.0)	3.27 (1.10 - 9.75)	< 0.05
previous admission (< 90 days)	18 (64.0)	17 (56.0)	1.38 (0.48 - 3.96)	0,37
mechanical ventilation	20 (71.0)	16 (53.0)	2.19 (0.74 - 6.50)	0,12
central venous catheter	22 (78.0)	22 (73.0)	1.33 (0.40 - 4.48)	0,43
vesical urinary catheter	23 (82.0)	17 (55.0)	3.52 (1.05 - 11.76)	< 0.05
elective surgery	20 (71.0)	14 (46.0)	2.86 (0.96 - 8.49)	< 0.05



Quem tem bactéria MDR? – CR - Pseudomonas

Characteristic	Carbapenem-resistant (n = 29)	Carbapenem-susceptible (n = 48)	OR (95%CI)	p
Age-years				
Mean	46.4 ± 22.71	49.0 ± 20.4		0.601
Gender-n (%)				
Male	22 (75.9)	34 (70.8)	1.30 (0.45–3.85)	0.418
Female	7 (24.1)	14 (29.2)		
Coexisting diseases-n (%)				
Comorbidities	12 (41.4)	29 (60.4)	0.46 (0.18–1.19)	0.083
Diabetes mellitus	4 (13.8)	7 (14.6)	0.94 (0.24–3.57)	0.602
Chronic renal failure	4 (13.8)	6 (12.5)	1.12 (0.29–3.57)	0.565
Heart failure	0 (0.0)	2 (4.2)	*	0.386
Hypertension	6 (20.7)	13 (27.1)	0.70 (0.23–2.13)	0.364
COPD	1 (3.4)	1 (2.1)	1.69 (0.10–33.33)	0.614
Cancer	2 (6.9)	9 (18.8)	0.32 (0.06–1.61)	0.134
Trauma	12 (41.4)	11 (22.9)	2.38 (0.88–6.67)	0.073
Burn	3 (10.3)	9 (18.8)	0.50 (0.12–2.04)	0.259
Hospitalization before <i>Pseudomonas</i> -days	24.6 ± 20.9	19.6 ± 18.6		0.66
Total duration of hospitalization-days	43.0 ± 31.7	43.1 ± 31.2		0.987
Other factors-n (%)				
Intensive care unit	24 (82.8)	25 (52.1)	4.55 (1.45–14.29)	0.006
Previous hospitalization	7 (24.1)	16 (33.3)	0.64 (0.22–1.82)	0.277
Previous <i>Pseudomonas</i> colonization	14 (48.3)	14 (29.2)	2.27 (0.97–6.25)	0.075
Mechanical ventilation	23 (79.3)	29 (60.4)	2.56 (0.87–7.69)	0.070
Central venous catheter	25 (86.2)	37 (77.1)	1.89 (0.53–6.67)	0.251
Urinary catheter	26 (89.7)	39 (81.3)	2.00 (0.50–8.33)	0.259
Surgery	4 (13.8)	8 (16.7)	0.80 (0.22–2.94)	0.503
Laboratory values-mean ± SD				
Hemoglobin (g/dL)	10.3 ± 2.0	10.0 ± 2.2		0.608
Leucocytes (1000 × cells/mm ³)	15.8 ± 9.0	11.9 ± 6.9		0.035
Immature cells (%)	17.2 ± 14.1	17.8 ± 14.0		0.853
Platelets (1000 × cells/mm ³)	184.4 ± 152.1	169.7 ± 173.3		0.778
Creatinine (mg/dL)	1.5 ± 1.7	1.8 ± 2.3		0.459
Previous antibiotic use	22 (75.9)	29 (60.4)	2.08 (0.74–5.88)	0.127
3rd and 4th generation cephalosporin	13 (44.8)	15 (31.3)	1.82 (0.69–4.76)	0.170
3rd generation cephalosporin	5 (17.2)	9 (18.8)	0.91 (0.27–3.03)	0.561
4th generation cephalosporin	10 (34.5)	8 (16.7)	2.63 (0.90–8.33)	0.067
Piperacillin/tazobactam	4 (13.8)	6 (12.5)	1.12 (0.29–4.55)	0.565
Quinolone	1 (3.4)	2 (4.2)	0.83 (0.07–10.00)	0.684
Carbapenem	20 (69.0)	17 (35.4)	4.17 (1.52–11.11)	0.004
Ertapenem	9 (31.0)	10 (20.8)	1.72 (0.60–5.00)	0.230
Imipenem or meropenem	15 (51.7)	14 (29.2)	2.63 (1.00–7.14)	0.042
Overall mortality	13 (44.8)	26 (54.2)	0.68 (0.27–1.73)	0.288

UTI

Uso de ceftriaxona

Uso de meropenem

BRAZ J INFECT DIS. 2012;16(4):351-356



The Brazilian Journal of
INFECTIOUS DISEASES

www.elsevier.com/locate/bjid



Original article

Risk factors for pan-resistant *Pseudomonas aeruginosa* bacteremia and the adequacy of antibiotic therapy

Felipe F. Tuon^{a,*}, Lucas W. Gortz^a, Jaime L. Rocha^b

**Table 1 – Univariate analysis of risk factors for CP-producing *Klebsiella pneumoniae* bacteremia.**

Variables	Cases (n = 18)	Controls (n = 67)	p
Age, years	60.4 ± 14.0	48.2 ± 16.6	0.005
Gender, male	11 (61.1)	38 (56.7)	0.95
Comorbidities			
Cardiovascular	3 (16.7)	28 (41.8)	0.04
Malignancy	3 (16.7)	9 (13.4)	0.49
Diabetes	10 (55.6)	17 (25.4)	0.03
Renal	1 (5.6)	10 (14.9)	0.27
Trauma	5 (27.8)	15 (22.4)	0.87
Previous surgery	7 (38.9)	38 (56.7)	0.28
Intensive care unit stay	14 (77.8)	44 (65.7)	0.25
Mechanical ventilation	16 (88.9)	34 (50.7)	0.003
Length of hospital stay*	28 (16–75)	32 (17–63)	0.99
Previous hospital admission	5 (27.8)	20 (29.9)	0.91
Antibiotic exposure			
Carbapenems	8 (44.4)	20 (29.9)	0.38
Cefepime	2 (11.1)	18 (26.9)	0.14
Ceftriaxone	4 (22.2)	10 (14.9)	0.34
Fluorquinolones	4 (22.2)	1 (1.5)	0.007
Vancomycin	4 (22.2)	13 (19.4)	0.51
Metronidazol	4 (22.2)	9 (13.4)	0.30
Presence of device			
Urinary catheter	17 (94.4)	44 (65.7)	0.01
Central venous catheter	17 (94.4)	36 (53.7)	0.001

Original article

Risk factors for KPC-producing *Klebsiella pneumoniae* bacteremia

Felipe F. Tuon^{a,b,*}, Jaime L. Rocha^c, Paula Toledo^{b,d}, Lavinia N. Arend^e, Camila H. Dias^a,
Talita M. Leite^a, Sergio R. Penteado-Filho^a, Marcelo Pilonetto^e, Alexandre P. Zavascki^f





Uso de antibióticos é fator de risco para resistência?

- CR-Pseudomonas

TABLE 2 Summary of studies ($n = 8$) regarding *P. aeruginosa* bacteremia, reporting risk factors for transmission and acquisition of carbapenem-resistant *P. aeruginosa*, based on multivariate analyses^a

Study ^c	Country	Study design	Hospital setting	No. of cases	Quality score ^b	Risk factors		OR estimate	95% CI	P value
						For what	Factor			
Joo, 2011 (73)	South Korea	cc	mix	46	4	imp	<u>Aminoglycoside use</u>	3.60	1.39–7.31	0.025
							Urinary catheter	3.19	1.39–7.31	0.006
							<u>Carbapenem use</u>	2.87	1.26–6.56	0.012
							<u>Fluoroquinolone use</u>	2.54	1.08–5.96	0.033
Tumbarello, 2011 (74)	Italy	cc	mix	106	6	mr	Central venous catheter	17.99	6.45–50.09	<0.001
							Previous antibiotic therapy	2.79	1.10–7.07	0.03
							Corticosteroid use	2.73	1.06–7.00	0.03
Yang, 2011 (75)	South Korea	cc	pea	7	4	mr	Admission to ICU	6.82	1.3–35.8	0.023
Johnson, 2009 (76)	USA	rc	mix	113	7	mr	Hospital-acquired BSI	2.41	1.39–4.18	0.002
							Previous transplantation	2.38	1.51–3.76	<0.001
							Admission to ICU	2.04	1.15–3.63	0.015
Tam, 2007 (77)	USA	cc	mix	18	4	car	Additional wk of hospitalization	1.25	1.04–1.51	0.019
Falagas, 2006 (78)	Greece	cc	mix	16	4	mr	<u>Carbapenem use</u>	9.0	2.4–34.3	0.001
Kang, 2005 (79)	South Korea	rc	mix	28	6	imp	<u>Carbapenem use</u>	40.96	8.92–188.3	<0.001
							<u>Fluoroquinolone use</u>	5.60	1.64–19.11	0.006
							Invasive procedure within previous 72 h	4.51	1.56–13.04	0.005
El Amari, 2001 (80)	Switzerland	cc	mix	81	4	mr	Previous monotherapy (including imipenem)	2.5	1.3–4.8	0.006



Além da falta de evidência....

- Qual é a plausibilidade?
 - Resistência a Carbapenems
 - Natural

**Principal forma de
aquisição de KPC,
OXA-23, SPM-1 é
transmissão
cruzada**

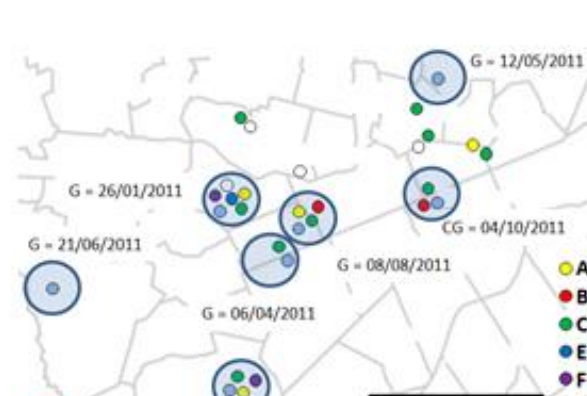
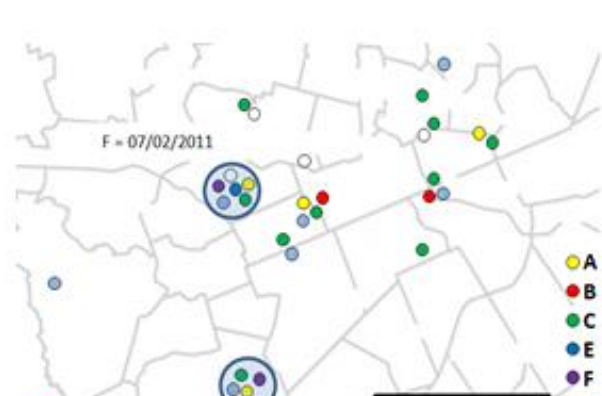
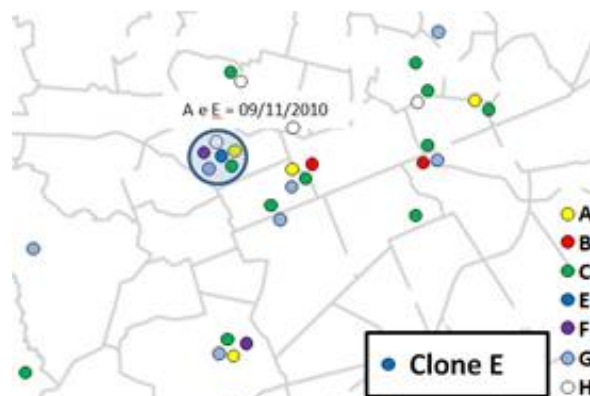
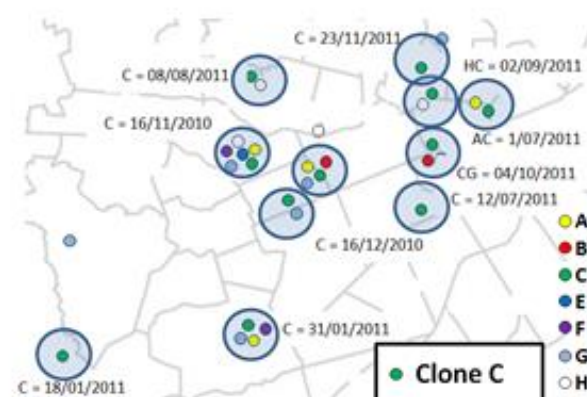
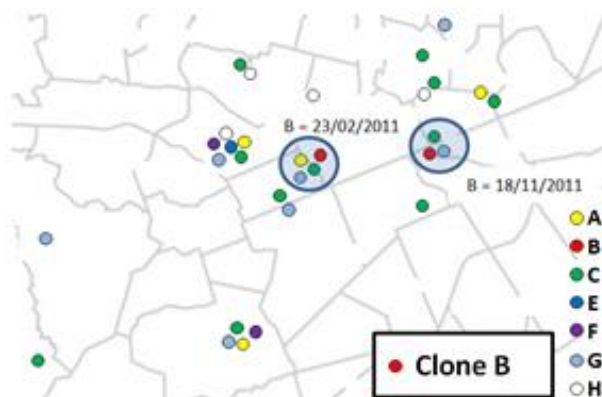
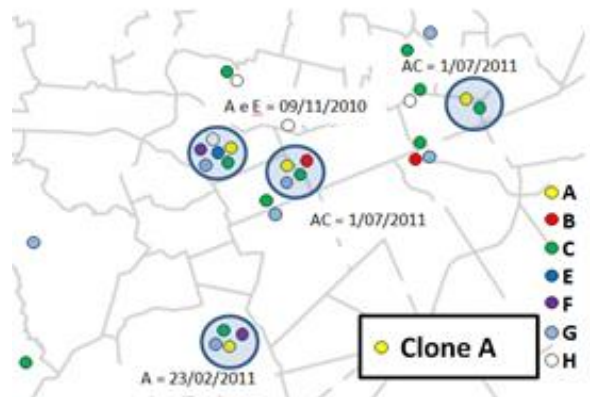
Resistência

Seleciona resistência



Expansão clonal de KPC em Curitiba

- Evitar transmissão cruzada seria mais importante?





Quanto tempo eu pego MDR?

SETOR	COLETA	DATA DE RECEBIMENTO	AMOSTRA	RESULTADO
UTI 1	1º COLETA	01/nov	SWAB	SERRATIA MARCESCENS MULTI-S
UTI 1	1º COLETA	01/nov	RASPADO	SERRATIA MARCESCENS MULTI-S
UTI 1	1º COLETA	01/nov	SWAB	EM ANDAMENTO
UTI 1	1º COLETA	01/nov	RASPADO	EM ANDAMENTO
UTI 3	1º COLETA	11/set	SWAB	NEGATIVO
UTI 3	1º COLETA	11/set	RASPADO	NEGATIVO
UTI 1	1º COLETA	02/out	SWAB	MRSA
UTI 1	1º COLETA	02/out	RASPADO	MRSA
UTI 3	1º COLETA	02/out	SWAB	NEGATIVO
UTI 3	1º COLETA	02/out	RASPADO	MRSA
UTI 1	1º COLETA	04/out	SWAB	NEGATIVO
UTI 1	1º COLETA	04/out	RASPADO	K.PNEUMONIAE CARBAP SENSÍVEL
UTI 3	1º COLETA	04/out	SWAB	NEGATIVO
UTI 3	1º COLETA	04/out	RASPADO	NEGATIVO
UTI 1	1º COLETA	04/out	SWAB	P.AERUGINOSA CARBAP S
UTI 1	1º COLETA	04/out	RASPADO	P.AERUGINOSA CARBAP S
UTI 1	1º COLETA	14/out	SWAB	MRSA
UTI 1	1º COLETA	14/out	RASPADO	AbMR + MRSA
UTI 3	1º COLETA	17/out	SWAB	AbMR
UTI 3	1º COLETA	17/out	RASPADO	NEGATIVO
UTI3	1º COLETA	22/out	SWAB	K.pneumoniae Multi S
UTI3	1º COLETA	22/out	RASPADO	AbMR
UTI3	1º COLETA	04/nov	SWAB	EM ANDAMENTO
UTI3	1º COLETA	04/nov	RASPADO	EM ANDAMENTO



Quanto tempo eu pego MDR?

3ª COLETA	06/out	SWAB
3ª COLETA	06/out	RASPADO
3ª COLETA	08/out	SWAB
3ª COLETA	08/out	RASPADO
3ª COLETA	08/out	SWAB



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DMR + MRSA
DMR + MRSA
TEUS MIRABILIS
TEUS MIRABILIS
NII CARBAP R + MRSA
NII CARBAP R + MRSA
MANNII CARBAP R
MANNII CARBAP R
Pmirabilis+MRSA



Além da falta de evidência científica...

- Existem outros fatores além dos antibióticos:
 - Maior gravidade dos pacientes atualmente
 - Maior imunossupressão
 - Maior uso de dispositivos invasivos
 - Alta incidência na comunidade de MDR, XDR e PDR
 - Adesão baixa ao isolamento
 - Dx tardio de MDR nos hospital
 - Técnicas demoradas de identificação
 - Uso de antibióticos de má qualidade na comunidade

Emergence and Rapid Regional Spread of *Klebsiella pneumoniae* Carbapenemase–Producing *Enterobacteriaceae*

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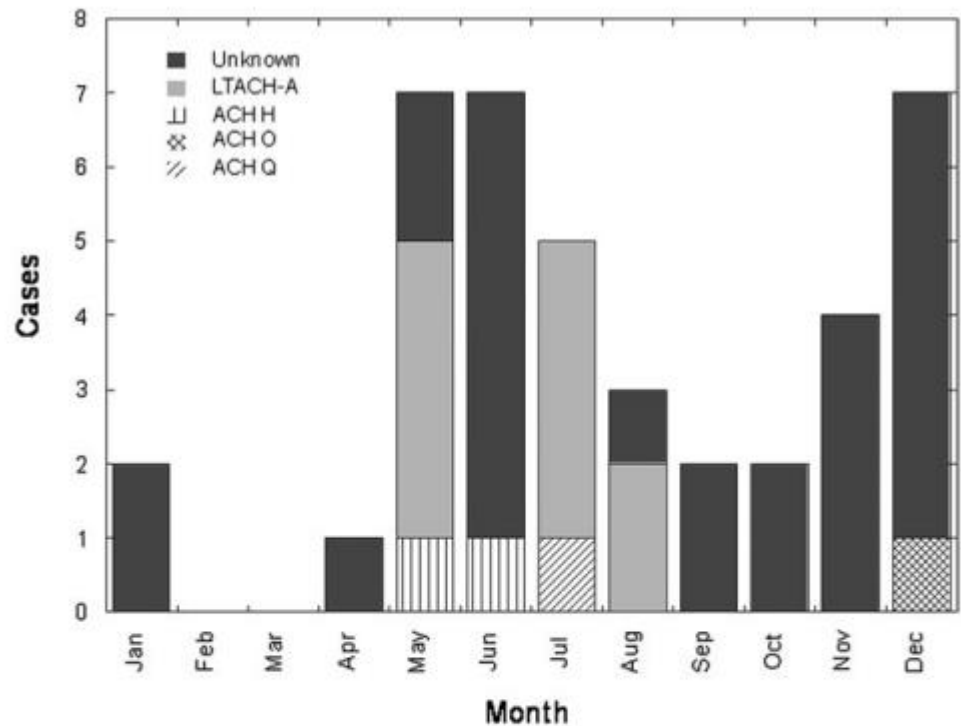
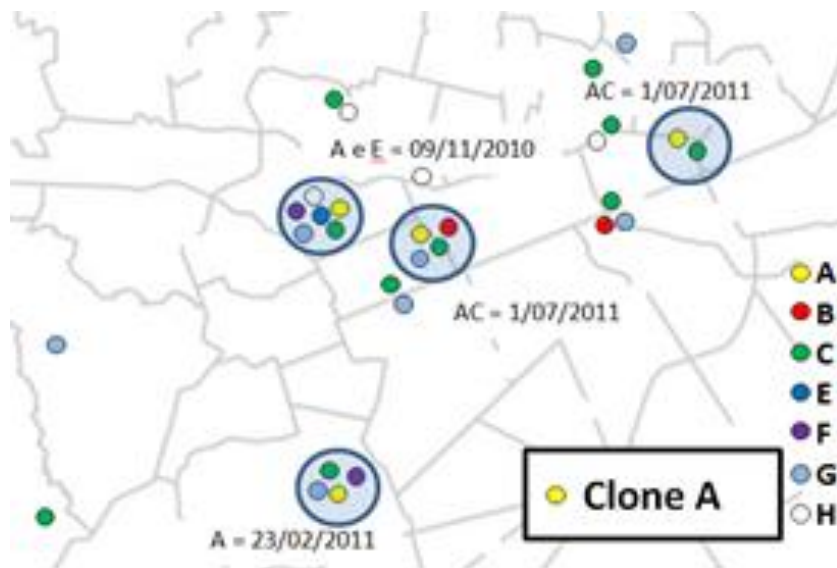
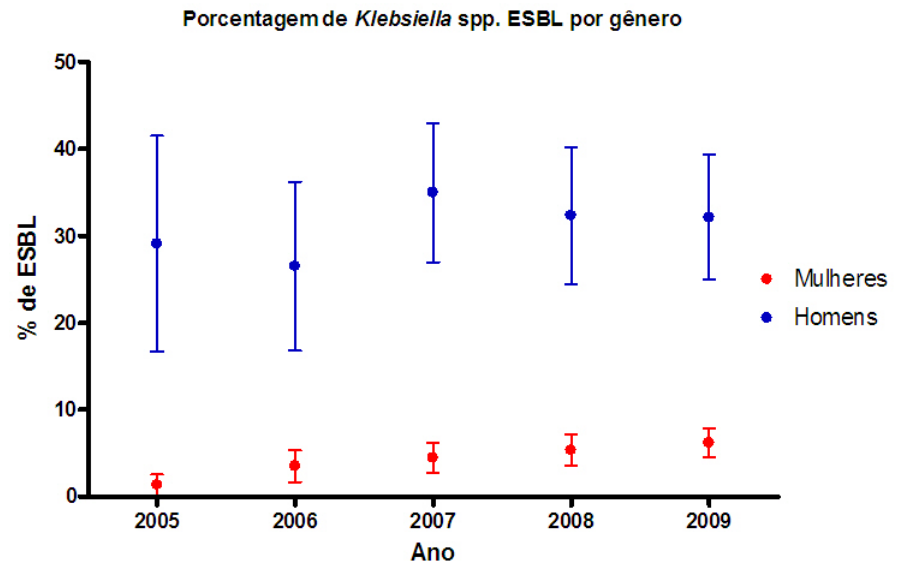
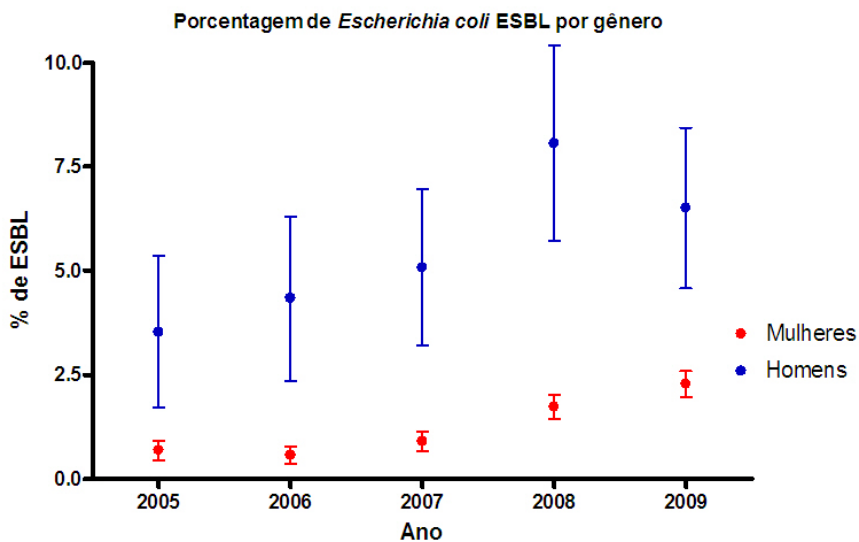


Figure 2. Epidemic curve of 40 patients that were colonized or infected with *Klebsiella pneumoniae* carbapenemase (KPC)–producing *Enterobacteriaceae*. Facility of acquisition of KPC-producing *Enterobacteriaceae* is indicated when known. LTACH-A, long-term acute care facility A; ACH H, acute care hospital H; ACH O, acute care hospital O; ACH Q, acute care hospital Q.



Atenção

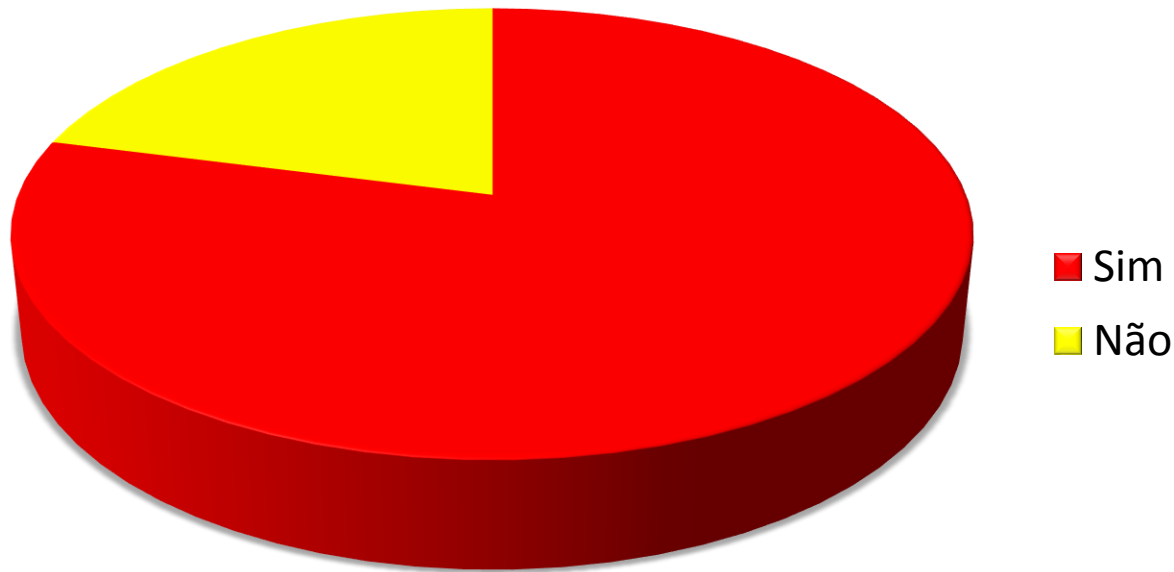
- “Ela está no meio de nós”
- Aumento de MDR na comunidade





Baixa adesão ao isolamento de contato


- 321 observações ($\approx 20\%$ de quebra do isolamento)





Faltam evidências...

- Por que faltam evidências sobre resistência?
 - Os PRAs são direcionados para “cost saving”
 - Diminuir uso?
 - OK
 - Menos carbapenems?



**Quer usar menos
carbapenem?
Pergunte-me como**



Ertapenem


- Ertapenem reduz resistência de *Pseudomonas aeruginosa* aos carbapenêmicos?
 - 2 revisões sistemáticas
 - Não há mudança de resistência
 - *Pseudomonas*
 - *Acinetobacter*
 - Enterobacteriaceae



Setting	Study period (addition of ertapenem)	Ertapenem use (DDD)	Group 2 carbapenem use (DDD before/after ^a)	% carbapenem susceptible (pre versus post ertapenem introduction)
Single centre, ca. 300-bed tertiary centre/teaching hospital; USA [16] ^b	March 2004 to December 2008 (July 2005)	58.4/1000 PD	37.5 to 21.0/1000 PD	<i>Pseudomonas</i> , 62.2 vs. 70.4 ($P = N/S$) Enterobacteriaceae, 82.5 vs. 88.6 ($P = N/S$)
Single centre, 344-bed teaching hospital; USA [6] ^c	January 2002 to December 2005 (July 2003)	44/1000 PD (median)	30 to 25/1000 PD (median)	<i>Pseudomonas</i> , 69 vs. 88 Enterobacteriaceae, no change
Single centre, 770-bed teaching hospital; USA [7]	January 2002 to December 2007 (May 2003)	3.4 to 8.9/1000 PD	21.5 to 31.1/1000 PD	<i>Pseudomonas</i> , 69 vs. 88 Enterobacteriaceae, no change
Single centre, 770-bed teaching hospital; USA [14]	January 2003 to December 2008 (May 2003)			
Retrospective, longitudinal hospital database study of nine medical wards (400 beds, 139 185 patient admissions, 504 ward months); Israel [15] ^d	2001 to 2005 (2001)	2130	4637	<i>Pseudomonas</i> , 3.8% annual increase in imipenem-resistant <i>Pseudomonas</i> ($P = 0.001$), associated only with group 2 carbapenem use ($P = 0.0014$)
Single-centre study using pharmacy purchase records and microbiology reports; USA [13]	2000 to 2007 (2003)	1670 (2003 to 2007)	1650 to 2295	<i>Pseudomonas</i> , 73.2 vs. 71.9 ($P = N/S$) (imipenem); 76.6 vs. 71.9 ($P = 0.0001$) (meropenem)
Single centre, 200-bed tertiary care centre; Brazil [10,11]	March 2005 to March 2007 (March 2006)	42.6/1000 PD	46.3 to 16.1/1000 PD	<i>Pseudomonas</i> , 20 to 0 ($P = N/S$)
Single centre, 200-bed, tertiary care centre; Brazil [12]	April 2006 to March 2008 (2006)	31.5/1000 PD	61.1 to 48.7 DDD/1000 PD	<i>Pseudomonas</i> , <i>Acinetobacter</i> , Enterobacteriaceae, no change
Multicentre (25 community and teaching hospitals), retrospective, data analysis; USA [8,9]	January 2000 to December 2008	7.3 to 15.9 ^e	10.4 to 15.3 ^e	<i>Pseudomonas</i> , 85.4 to 81.0 ($P = N/S$)




- Ertapenem





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Volume 62, Issue 3, March 2011, Pages 246–249



Letter to the Editor

Should polymyxin be used empirically to treat infections in patients under high risk for carbapenem-resistant *Acinetobacter*?

Felipe F. Tuon  

Andrea M. Rymsza

Sergio R. Penteado-Filho

Marcelo Pilonetto

Lavinia N. Arend

*10% de KP-
KPC
Resistentes a
PoliB*





Journal of Infection

Volume 67, Issue 3, September 2013, Pages 247–249



Letter to the Editor

Fosfomycin susceptibility of isolates with blaKPC-2 from Brazil

Felipe F. Tuon  

Jaime L. Rocha

Marina S. Formighieri, Samiria Sfair, Mariana B. Bertoldi

Jussara Kasuko Palmeiro

Libera Maria Dalla Costa



- Por que a incidência de MDR aumenta?
- Infecção precoce – Transmissão cruzada?
- É custo efetivo?
 - Ertapenem
 - Tigeciclina
 - Piperacilina/tazobactam
 - Cefepima
 - Qualidade de genéricos?

Generic Vancomycin Products Fail *In Vivo* despite Being Pharmaceutical Equivalents of the Innovator^V

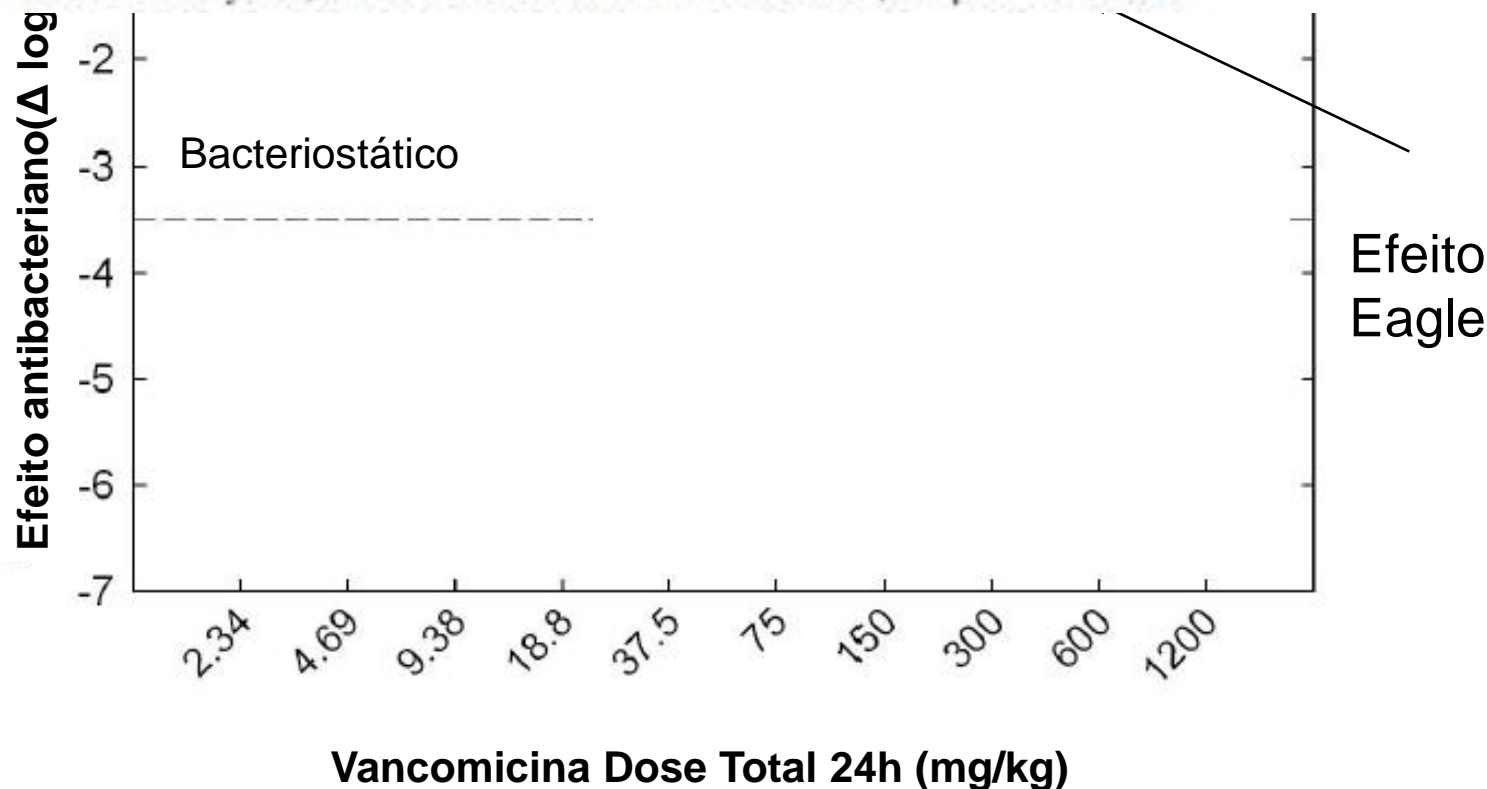
Omar Vesga,^{1,2*} Maria Agudelo,^{1,3} Beatriz E. Salazar,^{1,4}
Carlos A. Rodriguez,^{1,3} and Andres F. Zuluaga^{1,5}

GRIFE (Grupo Investigador de Problemas en Enfermedades Infecciosas),¹ Section of Infectious Diseases, Departments of Internal Medicine and Pharmacology,² Biomedical Sciences Corporation,³ Department of Microbiology and Parasitology,⁴ and Department of Pharmacology and Toxicology,⁵ University of Antioquia Medical School, Medellin, Colombia

Received 24 July 2009/Returned for modification 23 October 2009/Accepted 1 June 2010

Baxter

Abbot





[Diagn Microbiol Infect Dis](#). 2013 May;78(1):110-2. doi: 10.1016/j.diagmicrobio.2013.01.024. Epub 2013 Mar 13.

More potency assay results for generic non-USA lots of piperacillin/tazobactam and initial reports for generic meropenem compounds marketed in the USA.

[Jones RN¹](#), [Sader HS](#), [Flamm RK](#), [Watters AA](#).

⊕ Author information

Abstract

An ongoing program of international generic antimicrobial potency assays for piperacillin/tazobactam has been summarized here through December 2010, and the initial results for meropenem generic lots from the United States are also presented. Fifteen additional piperacillin/tazobactam generic lots revealed an average of -10% activity (range, +3 to -23%) compared to the branded product (Zosyn®; Wyeth-Pfizer), a finding consistent with prior reports (46 lots) of -16%. In contrast, meropenem branded and generic products had equivalent assay results (5 generic lots from 2 manufacturers [Hospira and Sandoz]). In conclusion, potencies for generic lots of parenteral broad-spectrum β -lactams can vary widely when directly compared to branded products, requiring documentation by chemical, in vitro activity (potency assays as measured here), and purity testing before considering their addition to a hospital formulary.

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[Br J Clin Pharmacol](#). 2009 Jul;88(1):34-42. doi: 10.1111/j.1365-2125.2009.03399.x.

Lack of pharmacokinetic bioequivalence between generic and branded amoxicillin formulations. A post-marketing clinical study on healthy volunteers.

[Del Tacca M¹](#), [Pasqualetti G](#), [Di Paolo A](#), [Virdis A](#), [Massimetti G](#), [Gori G](#), [Versari D](#), [Taddei S](#), [Blandizzi C](#).

⊕ Author information

Abstract

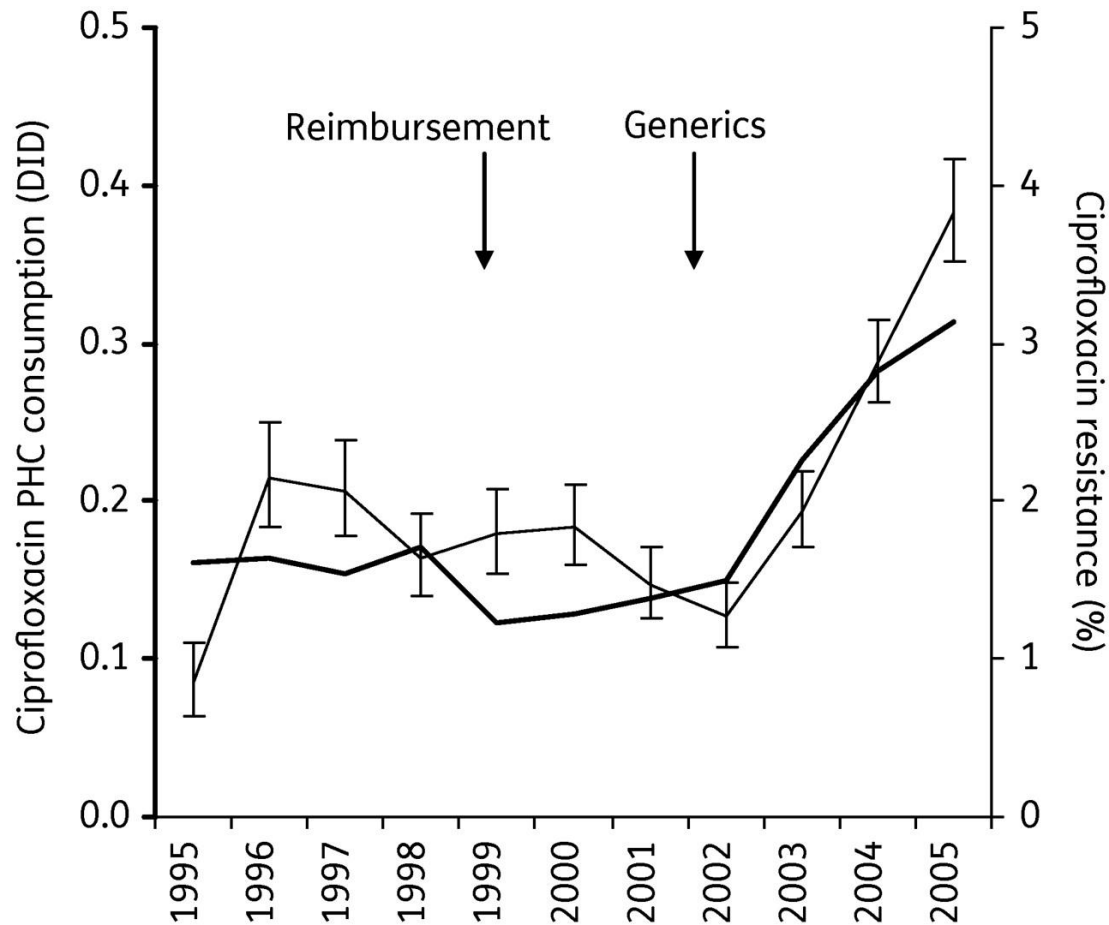
AIMS: There are concerns about the quality of generic drugs in the postmarketing setting. The aim was to establish whether two generic formulations of amoxicillin, available on the Italian market, fulfil the criteria for clinical pharmacokinetic bioequivalence vs. the branded drug.

METHODS: Two generic amoxicillin products (generic A and B) were selected among four fast-release tablet formulations available on the Italian market. Twenty-four healthy adult volunteers of either sex participated to a single-dose, randomized, three-treatment, crossover, single-blind bioequivalence study designed to compare generic A and B with branded amoxicillin. Plasma samples were collected at preset times for 24 h after dosing, and assayed for amoxicillin levels by high-performance liquid chromatography.

RESULTS: Ninety percent confidence intervals of AUC ratios were 0.8238, 1.0502 (ratio 0.9302) and 0.8116, 1.1007 (ratio 0.9452) for generic A and B vs. branded amoxicillin, respectively. Ninety percent confidence intervals of C(max) ratios were 0.7921, 1.0134 (ratio 0.8960) and 0.8246, 1.1199 (ratio 0.9610) for generic A and B vs. branded amoxicillin, respectively. The mean pharmacokinetic profiles showed that the AUC value of branded amoxicillin was 8.5 and 5.4% greater than that estimated for generic A and B, respectively. Few adverse events were recorded; these were not serious and occurred without apparent relationship to any specific amoxicillin formulation.

CONCLUSIONS: These results indicate that one of the two marketed amoxicillin generics analysed in the present study is not bioequivalent to the brand leader product for C(max) on the basis of single-dose pharmacokinetic assessment.

Trends in the frequency of ciprofloxacin resistance among *E. coli* urine isolates from PHC with 95% confidence intervals (thin line) and the consumption of ciprofloxacin by PHC patients from 1995 to 2005 in three to seven Danish counties (thick line) seen in the light of the removal of 50% reimbursement and the introduction of generics.



Jensen U S et al. *J. Antimicrob. Chemother.* 2010;65:1286-1291

Público vs Privado

Além de recursos humanos
e atitudes, será que
qualidade de medicamentos
não interfere?

Por que, pai?





- Evidência fraca como medida isolada
 - Qualidade ruim de estudos
- Não explica a colonização precoce
- Qual antibiótico restringir para evitar KPC, CRAB, CRPA?
 - Se Carba, qual alternativa?
 - Resistance saving ou cost saving (emprego saving?)
- Após décadas de uso não racional de antibióticos, hoje mudaremos as condutas?
 - Tarde demais?



November 30, 2010

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Eur J Med Res (2010) 15: 571-576

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MULTIRESISTANT BACTERIA AND CURRENT THERAPY – THE ECONOMICAL SIDE OF THE STORY

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Vol. 26 No. 6

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY

525

WHY IS IT THAT INTERNISTS DO NOT FOLLOW GUIDELINES FOR PREVENTING INTRAVASCULAR CATHETER INFECTIONS?



Lewis Rubinson, MD, PhD; Albert W. Wu, MD, MPH; Edward F. Haponik, MD; Gregory B. Diette, MD, MHS



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