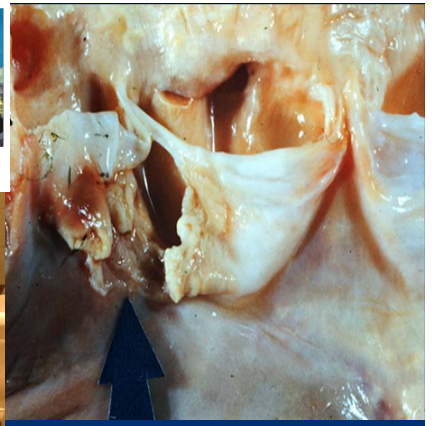
12th INTERNATIONAL SYMPOSIUM on MODERN CONCEPTS in ENDOCARDITIS and VASCULAR INFECTIONS



II CONGRESO
SEICAV
VII REUNIÓN
GAMES

BILBAO 2013
Palacio Euskalduna
27/28 de septiembre

TRATAMIENTO COMBINADO EN LA ENDOCARDITIS INFECCIOSA CAUSADA POR GRAMPOSITIVOS

¿ Que buscamos con la combinación de antibióticos en la EI ?

- 1.-Buscar un efecto sinérgico basado en diferentes mecanismos de acción
- 2.- Incrementar la rapidez de la muerte microbiológica
- 3.- Prevenir la emergencia de resistencias

INVITED ARTICLE CLINICAL PRACTICE

Ellie J. C. Goldstein, Section Editor

Combination Antibiotic Therapy for Infective Endocarditis

Thuan Le and Arnold S. Bayer

Research and Education Institute at Harbor–University of California, Los Angeles, Torrance, California

Clinical Infectious Diseases 2003; 36:615–21

Table 1. Clinical outcomes reported in selected studies of combination treatment for infective endocarditis (IE) due to common pathogens.

Reference	Study period or year of publication	Pathogen	Combination regimen	No. of episodes of IE	Valve(s) involved	Comments
Wilson et al. [27]	1972–1979	VGS	Pen + Stm	91	MV/AV	Two-week course of therapy; no cases of relapse
Francioli et al. [28]	1995	VGS	Ctri + Net	48	MV/AV	Short-course (2-week) therapy with single daily doses had outcome similar to 4-week courses [29–31]
Sexton et al. [32]	1992–1995	VGS	Ctri + Gm vs. Ctri	51	MV/AV	Short-course (2-week) combination therapy had outcome similar to 4-week monotherapy
Korzeniowski et al. [33]	1982	SA	Naf + Gm vs. Naf	19	TV	No differences observed
			Naf + Gm vs. Naf	15	MV/AV	Naf + Gm was superior to Naf alone for bacteremia clearance
Watanakunakorn et al. [34]	1961–1975	SA	CWA + Gm vs. CWA	40	MV/AV/TV	No differences observed
Abrams et al. [35]	1976–1977	SA	CWA + Gm vs. CWA	25	TV	No differences observed
Dworkin et al. [36]	1989	SA	Cpfx (po) + Rif (po)	14	TV	100% Cure rate in 10 assessable patients
Chambers et al. [37]	1983–1987	SA	Naf + Tm	50	TV	94% Cure rate for short-course (2-week) therapy
Heldman et al. [38]	1990–1993	SA	Cpfx (po) + Rif (po) vs. Oxa + Gm	85	TV	Cure rates, 95% vs. 88%
Ribera et al. [39]	1988–1993	SA	Clox vs. Clox + Gm	90	TV	Cure rates, 92% vs. 94%
Fortun et al. [40]	2001	SA	Clox + Gm vs. Vm or Teic + Gm	31	TV	Cure rates, 100% vs. 60%–70%
Olaison et al. [41]	1995–1999	E	CWA + AG	93	MV/AV	82% Cure rate with shortened duration of AG therapy (median, 15 days)
Gavalda et al. [42]	2001	E	Amp + Ctri or Ctax	20	MV/AV	100% Cure rate

- Discrepancia entre la sinergia in vitro de muchos betalactamicos con aminoglucósidos en combinación y los resultados obtenidos en estudios clínicos randomizados controlados

Salvo en la EI enterococica el efecto sinérgico ha demostrado escasamente su eficacia

Moellering et al. Synergy of penicillin and gentamicin against enterococci. J Infect Dis 1971

Journal of Antimicrobial Chemotherapy (2006) **57**, 639–647
doi:10.1093/jac/dkl044
Advance Access publication 24 February 2006

JAC

The role of aminoglycosides in combination with a β-lactam for the treatment of bacterial endocarditis: a meta-analysis of comparative trials

Matthew E. Falagas[1,2]*, Dimitrios K. Matthaiou[1] and Ioannis A. Bliziotis[1]

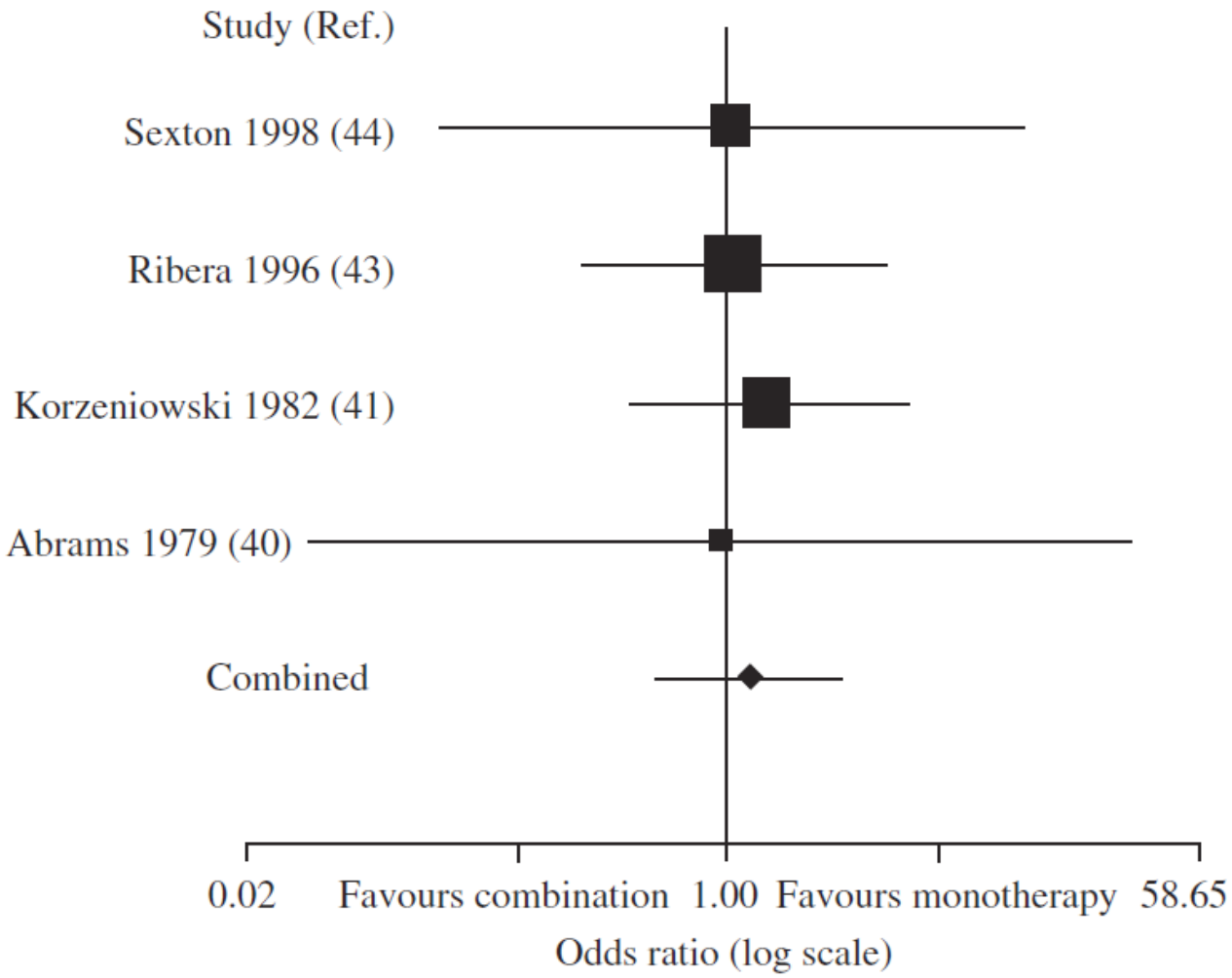


Figure 2. Odds ratios of clinical cure (treatment success) between patients who received β-lactam monotherapy and those who received β-lactam/aminoglycoside combination therapy. Vertical line = 'no difference' point in treatment success between the two regimens. Horizontal lines = 95% CI. Square = odds ratio; the size of each square denotes the proportion of information given by each trial. Diamond = pooled odds ratio for all studies.

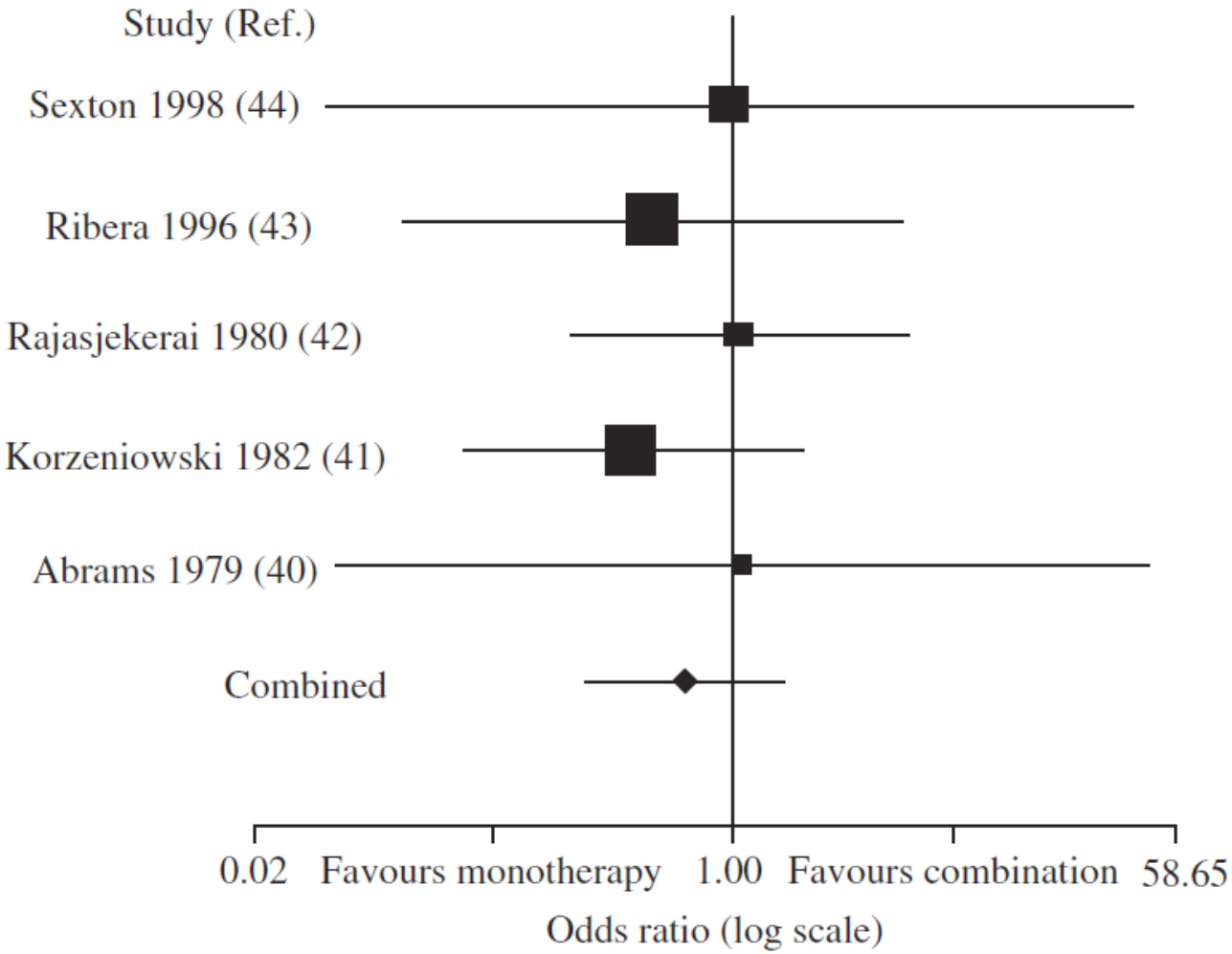


Figure 3. Odds ratios of all-cause mortality between patients who received β-lactam monotherapy and those who received β-lactam/aminoglycoside combination therapy. Vertical line = 'no difference' point in all-cause mortality between the two regimens. Horizontal lines = 95% CI. Square = odds ratio; the size of each square denotes the proportion of information given by each trial. Diamond = pooled odds ratio for all studies.

The role of aminoglycosides in combination with a β-lactam for the treatment of bacterial endocarditis: a meta-analysis of comparative trials

Matthew E. Falagas[1,2]*, Dimitrios K. Matthaiou[1] and Ioannis A. Bliziotis[1]

Limitaciones del estudio

- Numero de estudios y de pacientes relativamente pequeño
- Distintas definiciones de endocarditis
- En solo 2 estudios monotorizada gentamicina
- No evaluados otra datos como tiempo de defervescencia ni toxicidad con régimen comparador

International Journal of Antimicrobial Agents 36S (2010) S46–S49

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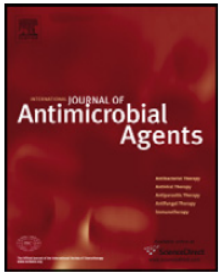
journal homepage: http://www.elsevier.com/locate/ijantimicag



Aminoglycoside-containing antibiotic combinations for the treatment of bacterial endocarditis: an evidence-based approach

Leonard Leibovici[a,b,*]

[a] *Department of Medicine E, Rabin Medical Center, Beilinson Hospital, Petah-Tiqva, Israel*
[b] *Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel*

Table 2
Randomised controlled trials comparing β-lactam monotherapy with the addition of an aminoglycoside in bacterial endocarditis and Gram-positive bacteraemia.

Study	Pathogen	Patients	Duration
Sexton [9]	*Streptococcus bovis* or viridans streptococci	Endocarditis	4 weeks vs. 2 weeks
Ribera [10]	*Staphylococcus aureus*	Endocarditis in drug users	2 weeks
Korzeniowski [11]	*S. aureus*	Endocarditis	6 weeks
Abrams [12]	*S. aureus*	Endocarditis in drug users	4 weeks
Coppens [13]	*S. aureus*	Bacteraemia	>1 week

Recomendaciones sociedades científicas

AHA Scientific Statement

Infective Endocarditis

Diagnosis, Antimicrobial Therapy, and Management of Complications

A Statement for Healthcare Professionals From the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association

Endorsed by the Infectious Diseases Society of America

Larry M. Baddour, MD, Chair; Walter R. Wilson, MD; Arnold S. Bayer, MD; Vance G. Fowler, Jr, MD, MHS; Ann F. Bolger, MD; Matthew E. Levison, MD*; Patricia Ferrieri, MD; Michael A. Gerber, MD; Lloyd Y. Tani, MD; Michael H. Gewitz, MD; David C. Tong, MD; James M. Steckelberg, MD; Robert S. Baltimore, MD†; Stanford T. Shulman, MD; Jane C. Burns, MD; Donald A. Falace, DMD‡; Jane W. Newburger, MD, MPH; Thomas J. Pallasch, DDS, MS; Masato Takahashi, MD; Kathryn A. Taubert, PhD

Circulation 2005

European Heart Journal (2009) **30**, 2369–2413
doi:10.1093/eurheartj/ehp285

ESC GUIDELINES

Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009)

The Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC)

J Antimicrob Chemother 2012; **67**: 269–289
doi:10.1093/jac/dkr450 Advance Access publication 14 November 2011

Journal of Antimicrobial Chemotherapy

Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy

F. Kate Gould[1]*, David W. Denning[2], Tom S. J. Elliott[3], Juliet Foweraker[4], John D. Perry[1], Bernard D. Prendergast[5], Jonathan A. T. Sandoe[6], Michael J. Spry[1] and Richard W. Watkin[7]

Endocarditis estreptococicas

Tratamiento de la EI causada por **Streptococcus viridans**

- Todas las guías diferencian según nivel de R a penicilina
- La actividad bactericida a penicilina G no se puede predecir cuando la CMI de **S. viridans** es > 0.12 µg/ml.
- Recomendación añadir gentamicina si la CMI es > 0.12 µg/ml
- Faltan estudios clínicos que demuestren su eficacia

Table 13 Antibiotic treatment of infective endocarditis due to oral streptococci and group D streptococci[a]

Antibiotic	Dosage and route	Duration (weeks)	Level of evidence
Strains fully susceptible to penicillin (MIC <0.125 mg/L)			
Standard treatment			
Penicillin G[b]	12–18 million U/day i.v. in 6 doses	4[c]	I B
or			
Amoxicillin[d]	100–200 mg/kg/day i.v. in 4–6 doses	4[c]	I B
or			
Ceftriaxone[e]	2 g/day i.v. or i.m. in 1 dose	4[c]	I B
	Paediatric doses:[f] Penicillin G 200,000 U/kg/day i.v. in 4–6 divided doses. Amoxicillin 300 mg/kg/day i.v. in 4–6 equally divided doses. Ceftriaxone 100 mg/kg/day i.v. or i.m. in 1 dose.		
Two-week treatment[(g)]			
Penicillin G	12–18 million U/day i.v. in 6 doses	2	I B
or			
Amoxicillin[d]	100–200 mg/kg/day i.v. in 4–6 doses	2	I B
or			
Ceftriaxone[e]	2 g/day i.v. or i.m. in 1 dose	2	I B
with			
Gentamicin[h]	3 mg/kg/day i.v. or i.m. in 1 dose	2	I B
or			
Netilmicin	4–5 mg/kg/day i.v. in 1 dose	2	I B
	Paediatric doses:[f] Penicillin, amoxicillin and ceftriaxone as above. Gentamicin 3 mg/kg/day i.v. or i.m. in 1 dose or in 3 equally divided doses.		
In beta-lactam allergic patients			
Vancomycin[i]	30 mg/kg/day i.v. in 2 doses	4[c]	I C
	Paediatric doses:[f] Vancomycin 40 mg/kg/day i.v. in 2–3 equally divided doses.		

Wilson WR, Thompson RL, Wilkowske CJ, Washington JA 2nd, Giuliani ER, Geraci JE. Short-term therapy for streptococcal infective endocarditis: combined intramuscular administration of penicillin and streptomycin. JAMA **1981**; 245:360–3.

Francioli P, Ruch W, Stamboulian D. Treatment of streptococcal endocarditis with a single daily dose of ceftriaxone and netilmicin for 14 days: a prospective multicenter study. Clin Infect Dis **1995**; 21:1406–10.

Ceftriaxone Once Daily for Four Weeks Compared with Ceftriaxone Plus Gentamicin Once Daily for Two Weeks for Treatment of Endocarditis Due to Penicillin-Susceptible Streptococci

Daniel J. Sexton, Marvin J. Tenenbaum, Walter R. Wilson, James M. Steckelberg, Alan D. Tice, David Gilbert, William Dismukes, Richard H. Drew, David T. Durack, and the Endocarditis Treatment Consortium Group

From the Division of Infectious Diseases, Department of Medicine, Duke University Medical Center, Durham, North Carolina; the North Shore University Hospital, Manhasset, New York; the Mayo Clinic, Saint Marys Hospital, Rochester, Minnesota; Infections Limited, Tacoma, Washington; the Providence Medical Center, Portland, Oregon; the University of Alabama, Birmingham, Alabama; and Becton Dickinson, Sparks, Maryland

Clinical Infectious Diseases 1998; 27:1470–4

Table 3. Clinical outcome for 51 evaluable patients with endocarditis due to penicillin-susceptible streptococci who were treated with monotherapy with ceftriaxone for 4 weeks or combination therapy with ceftriaxone plus gentamicin for 2 weeks.

	No. (%) of patients	
Clinical outcome	Monotherapy recipients ($n = 26$)	Combination therapy recipients ($n = 25$)
Cure without surgery	21 (80.8)	15 (60)
Cure with surgery	4 (15.4)	9 (36)
Treatment failure	1 (3.8)	1 (4)

Table 4. Microbiological outcome for 46 patients with endocarditis due to penicillin-susceptible streptococci who were treated with monotherapy with ceftriaxone for 4 weeks or combination therapy with ceftriaxone plus gentamicin for 2 weeks.

Microbiological outcome	No. (%) of patients	
	Monotherapy recipients* ($n = 23$)	Combination therapy recipients† ($n = 23$)
Cure	22 (95.7)	22 (95.7)
Reinfection	1 (4.3)	0
Treatment failure	0	1 (4.3)

* Three patients in this group were not evaluable for microbiological outcome.

† Two patients in this group were not evaluable for microbiological outcome.

MAJOR ARTICLE

Infective Endocarditis Due to Penicillin-Resistant Viridans Group Streptococci

Bettina Knoll,[1] Imad M. Tleyjeh,[3] James M. Steckelberg,[1,2] Walter R. Wilson,[1,2] and Larry M. Baddour[1,2]

[1]Department of Medicine and [2]Division of Infectious Diseases, Mayo Clinic College of Medicine, Rochester, Minnesota; and [3]Division of Infectious Diseases, Department of Medicine, King Fahd Medical City, Riyadh, Saudi Arabia

Clinical Infectious Diseases 2007; 44:1585–92

- Estudio retrospectivo de 29 pacientes con EI por S. viridans peni R (CMI >0,12 µg/ml) (AHA 2005)
- Clínica Mayo Enero 1967 - Abril 2006
- 65,5% válvulas nativas

MIC of penicillin, µg/mL	
0.5	9 (31.0)
1.0	16 (55.2)
2.0	2 (6.9)
4.0	2 (6.9)

Resultados

- Hasta año 1983 tratamiento penicilina + estreptomicina 2,3 ± 0,4 semanas. Curados 9 de 10 pacientes tratados

- Desde año 83 duración tratamiento 5,1 ± 1,4 semanas (2 primeras combinado y sigúientes en monoterapia). Curación 7 de 8

-
- EI protésica : 1 recibio vancomicina y 8 penicilina o ceftriaxona 4 semanas y aminoglucosido en tiempo, dosis y duración variable. Curación 9/10

Journal of Infection (2012) **64**, 127—129

ELSEVIER

LETTER TO THE EDITOR

Infective endocarditis caused by Group B *Streptococcus*: The role of aminoglycoside-combination

Table 1 The use of aminoglycosides in association with outcome in 74 episodes of infective endocarditis due to Group B *Streptococcus*.

	Duration of aminoglycoside treatment (days)			
	0	1–7	≥8	*P*
	n = 20 (27)	*n* = 16 (22)	*n* = 38 (51)	
Heart failure prior to treatment	5 (25)	5 (31)	9 (24)	ns
New heart failure during treatment	2 (10)[a]	4 (20)	14 (70)[a]	0.035
Ongoing or new heart failure during treatment	5 (25)[a]	7 (44)	21 (55)[a]	0.050
Days on ward, median (IQR)	36 (29–57)	33 (29–54)	32 (26–47)	ns
Mortality	1 (5)	4 (25)	5 (13)	ns

Data are no. (%) of cases, unless otherwise indicated. The episode numbers of each category (20, 16, and 38) were used as denominators. IQR, interquartile range.

[a] Heart failure was significantly more often present in patients that were treated with aminoglycoside for ≥8 days than in patients without aminoglycoside treatment.

Le Infezioni in Medicina, n. 2, 67-74, 2012

Rassegna

Review

Endocarditis caused by nutritionally variant streptococci: a case report and literature review

Endocardite da varianti nutrizionali streptococciche: descrizione di un caso e revisione della letteratura

Simone Giuliano[1], Roberta Caccese[2], Paolo Carfagna[2], Antonio Vena[1], Marco Falcone[1], Mario Venditti[1]

- Hasta 2001 alrededor 100 casos publicados
- 22 publicados desde 2001
- 78% peni s, cirugía 48%, mortalidad 9%
- Todos tratamiento combinado

DATOS GAMES (1000 EI)
193 EI Estreptococicas

- **CMI ≤ 0,12**
- 79 tratados
- Mortalidad
  12 (15%)

Combinado* 5 (10,4%)
Monoterapia 7 (22,6)

- **CMI 0,12-0,5**
- 18 tratados
- Mortalidad
  3 (16,7%)

Combinado 3 (23%)
Monoterapia 0

- **CMI ≥ 0,5**
- 97 tratados
- Mortalidad
  13 (13,4%)

Combinado 8 (14,3%)
Monoterapia 5 (12,2%)

Endocarditis enterococicas

Table 15 Antibiotic treatment of infective endocarditis due to *Enterococcus* spp.

Antibiotic	Dosage and route	Duration (weeks)	Level of evidence
Beta-lactam and gentamicin susceptible strain (for resistant isolates see[a,b,c])			
Amoxicillin *with* Gentamicin[e]	200 mg/kg/day i.v. in 4–6 doses 3 mg/kg/day i.v. or i.m. in 2 or 3 doses. ***Paediatric doses:***[f] Amoxicillin 300 mg/kg/day i.v. in 4–6 equally divided doses. Gentamicin 3 mg/kg/day i.v. or i.m. in 3 equally divided doses.	4–6[d] 4–6	I B
OR			
Ampicillin *with* Gentamicin[e]	200 mg/kg/day i.v. in 4–6 doses 3 mg/kg/day i.v. or i.m. in 2 or 3 doses ***Paediatric doses:***[f] Ampicillin 300 mg/kg/day i.v. in 4–6 equally divided doses. Gentamicin as above.	4–6[d] 4–6	I B
OR			
Vancomycin[g] *with* Gentamicin[e]	30 mg/kg/day i.v. in 2 doses 3 mg/kg/day i.v. or i.m. in 2 or 3 doses ***Paediatric doses:***[f] Vancomycin 40 mg/kg/day i.v. in 2–3 equally divided doses. Gentamicin as above.	6 6	I C

Enterococcal Endocarditis in Sweden, 1995–1999: Can Shorter Therapy with Aminoglycosides Be Used?

Lars Olaison and Kimmo Schadewitz for the Swedish Society of Infectious Diseases Quality Assurance Study Group for Endocarditis

Department of Infectious Diseases, Sahlgrenska University Hospital, Göteborg University, Göteborg, Sweden

Clinical Infectious Diseases 2002;34:159–66

93 episodios: mortalidad 16% recaídas 3%

Media duración tratamiento en curados:

42 días betalactamico + 2 semanas aminoglucosido

Reconsidera recomendaciones guías

Gavaldà J, Len O, Miró JM, Muñoz P, Montejo M, Alarcón A, et al. Brief communication: treatment of Enterococcus faecalis endocarditis with ampicillin plus ceftriaxone. Ann Intern Med. 2007 Apr 17;146(8):574-9

	Número de pacientes (%)		
	HLAR (n=21)	no HLAR (n=22)	Global (n=43)
Complicaciones	9 (43) p=0,021	16 (73)	25 (58)
- Fallo cardiaco	5 (24)	6 (27)	11 (26)
- Embolismo cerebral	1 (5)	5 (23)	6 (14)
- Absceso paravalvular	1 (5)	2 (9)	3 (7)
Fracaso	6 (29) p= ns	8 (36)	14 (33)
- Muerte	6 (29)	6 (27)	12 (28)
- Recidivas	0	2 (9) *	2 (5)

* Violación del protocolo en un paciente con y probable existencia de infección de injerto vascular en el otro

Ampicillin Plus Ceftriaxone Is as Effective as Ampicillin Plus Gentamicin for Treating *Enterococcus faecalis* Infective Endocarditis

Nuria Fernández-Hidalgo,[1] Benito Almirante,[1] Joan Gavaldà,[1] Mercè Gurgui,[2] Carmen Peña,[3] Arístides de Alarcón,[4] Josefa Ruiz,[5] Isidre Vilacosta,[6] Miguel Montejo,[7] Nuria Vallejo,[8] Francisco López-Medrano,[9] Antonio Plata,[10] Javier López,[11] Carmen Hidalgo-Tenorio,[12] Juan Gálvez,[13] Carmen Sáez,[14] José Manuel Lomas,[15] Marco Falcone,[18] Javier de la Torre,[16] Xavier Martínez-Lacasa,[17] and Albert Pahissa[1]

Clinical Infectious Diseases 2013;56(9):1261–8

Fernandez Hidalgo et al. Ampicillin Plus Ceftriaxone is a Effective as Ampicillin Plus Gentamicin for Treating Enterococcus faecalis Infective Endocarditis

Variable	Amp+Cef (n= 159)	Amp+Gen (n= 87)
Origen		
•Nosocomial	93 (59%)	35 (40%)
Localización		
•Aórtica	73 (46%)	37 (43%)
•Mitral	46 (29%)	32 (37%)
•Aortica y Mitral	30 (19%)	14 (16%)
Protésicas	59 (37%)	30 (34%)
Edad	70,4	69,8

Fernandez Hidalgo et al. Ampicillin Plus Ceftriaxone is a Effective as Ampicillin Plus Gentamicin for Treating Enterococcus faecalis Infective Endocarditis

	Número de pacientes (%)		
	AMP/CEF (n=159)	AMP/GEN (n=87)	
Complicaciones	120 (76)	72 (83)	
- Fallo cardiaco	87 (55)	54 (62)	
- Embolismo cerebral	25 (16)	14 (16)	
- Absceso paravalvular	36 (23)	22 (25)	
Cirugía indicada fase aguda	58%	65%	
-Muerte durante tratamiento	35 (22)	18 (21)	
-Muerte 3 meses seguimiento	13 (8)	6 (7)	
-Retirada antibiot reacción adversa	2 (1)	22 (25)	p<0.001
- Recidivas	3 (3)	3 (4)	

DATOS GAMES (1000 EI)
122 EI Enterocócicas

- **Ampicilina+Ceftriaxona**
- 61 tratados
- Mortalidad 14 (23%)

- **Ampicilina+Gentamicina**
- 30 tratados
- Mortalidad 6 (20%)

¿ Que hacer si falla la pauta Amp+Cef ?

- Retratamiento con la misma pauta ?
- Ampicilina + gentamicina si no alto nivel R
- Daptomicina 10-12mg/Kg
- Daptomicina + Ampicilina

EI nativa por S. aureus meti
S

Combination antimicrobial therapy for **Staphylococcus aureus** endocarditis in patients addicted to parenteral drugs and in a nonaddicts: a prospective study

Korzeniowski O, Sande MA. Ann Intern Med 1982

En 15 pacientes no ADVP con EI la asociación nafcilina con gentamicina fue superior a nafcilina sola en la rapidez de desaparición de la bacteriemia en 1-2 días, pero no en la mortalidad

MAJOR ARTICLE

Initial Low-Dose Gentamicin for *Staphylococcus aureus* Bacteremia and Endocarditis Is Nephrotoxic

Sara E. Cosgrove,[1] Gloria A. Vigliani,[2] Marilyn Campion,[a] Vance G. Fowler, Jr.,[5] Elias Abrutyn,[7,b] G. Ralph Corey,[5,6] Donald P. Levine,[8] Mark E. Rupp,[9] Henry F. Chambers,[10] Adolf W. Karchmer,[3] and Helen W. Boucher[4]

[1]Division of Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, Maryland; [2]Vigliani Consulting, Waban, and [3]Division of Infectious Diseases, Beth Israel Deaconess Medical Center, and [4]Division of Infectious Diseases, Tufts Medical Center, Boston, Massachusetts; [5]Division of Infectious Diseases, Duke University Medical School, and [6]Duke Clinical Research Institute, Durham, North Carolina; [7]Drexel University College of Medicine, Philadelphia, Pennsylvania; [8]Wayne State University, University Health Center, Detroit, Michigan; [9]Division of Infectious Diseases, University of Nebraska Medical Center, Omaha; and [10]Division of Infectious Diseases, University of California, San Francisco

Clinical Infectious Diseases 2009; 48:713–21

EDITORIAL COMMENTARY

Initial Low-Dose Aminoglycosides in *Staphylococcus aureus* Bacteremia: Good Science, Urban Legend, or Just Plain Toxic?

Arnold S. Bayer[1] and Barbara E. Murray[2]

[1]Department of Medicine, Geffen School of Medicine at University of California–Los Angeles; and [2]Division of Infectious Diseases and Center for the Study of Emerging and Re-emerging Pathogens, University of Texas Medical School at Houston

(See the article by Cosgrove et al. on pages 713–21)

EI S. aureus. Asociación rifampicina

- Mas duración bacteriemia por SARM si se asociaba con vancomicina
- Levine et al. Ann Intern Med 1991

- Mas duración bacteriemia ,mortalidad y efectos adversos en asociación. Si prótesis mas cultivo válvula negativo
- Drinkovic et al. JAC 2003
- Riedel et al. Antimicrob Agents Chemother 2008

Table 14 Antibiotic treatment of infective endocarditis due to *Staphylococcus* spp.

Antibiotic	Dosage and route	Duration (weeks)	Level of evidence
Native valves			
Methicillin-susceptible staphylococci:			
(Flu)cloxacillin *or* Oxacillin *with* Gentamicin[a]	12 g/day i.v. in 4–6 doses 3 mg/kg/day i.v. or i.m. in 2 or 3 doses ***Paediatric doses:***[b] Oxacillin or (Flu)cloxacillin 200 mg /kg/day i.v. in 4–6 equally divided doses. Gentamicin 3 mg/kg/day i.v. or i.m. in 3 equally divided doses.	4–6 3–5 days	I B
Penicillin-allergic patients or methicillin-resistant staphylococci:			
Vancomycin[c] *with* Gentamicin[a]	30 mg/kg/day i.v. in 2 doses 3 mg/kg/day i.v. or i.m. in 2 or 3 doses ***Paediatric doses:***[b] Vancomycin 40 mg/kg/day i.v. in 2–3 equally divided doses.	4–6 3–5 days	I B

J Antimicrob Chemother 2012; **67**: 269–289
doi:10.1093/jac/dkr450 Advance Access publication 14 November 2011

Journal of Antimicrobial Chemotherapy

Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy

F. Kate Gould[1]*, David W. Denning[2], Tom S. J. Elliott[3], Juliet Foweraker[4], John D. Perry[1], Bernard D. Prendergast[5], Jonathan A. T. Sandoe[6], Michael J. Spry[1] and Richard W. Watkin[7]

Recommendation 7.1: First-line therapy for methicillin-susceptible staphylococci is 2 g of flucloxacillin every 6 h, increasing to 2 g every 4 h in patients weighing >85 kg. [A]

This recommendation is unchanged from previous guidelines.

Recommendation 7.2: Gentamicin should not be added to flucloxacillin for the initial treatment of native valve staphylococcal IE. [A]

EI nativas derechas por S. aureus

Ribera [10]	*Staphylococcus aureus*	Endocarditis in drug users	2 weeks
Korzeniowski [11]	*S. aureus*	Endocarditis	6 weeks
Abrams [12]	*S. aureus*	Endocarditis in drug users	4 weeks

Dworkin et al. [36]	1989	SA	Cpfx (po) + Rif (po)	14	TV	100% Cure rate in 10 assessable patients
Chambers et al. [37]	1983–1987	SA	Naf + Tm	50	TV	94% Cure rate for short-course (2-week) therapy
Heldman et al. [38]	1990–1993	SA	Cpfx (po) + Rif (po) vs. Oxa + Gm	85	TV	Cure rates, 95% vs. 88%

Effectiveness of Cloxacillin with and without Gentamicin in Short-Term Therapy for Right-Sided *Staphylococcus aureus* Endocarditis

A Randomized, Controlled Trial

Esteban Ribera, MD; Jose Gómez-Jimenez, MD; Emilia Cortes, MD; Oscar del Valle, MD; Ana Planes, MD; M. Teresa Gonzalez-Alujas, MD; Benito Almirante, MD; Imma Ocaña, MD; and Albert Pahissa, MD

15 December 1996 • *Annals of Internal Medicine* • Volume 125 • Number 12

Table 4. Outcome of 74 Patients Evaluable for the Efficacy Analysis

Outcome	Cloxacillin-Only Group (n = 38)	Cloxacillin plus Gentamicin Group (n = 36)
Successful therapy, *n (%)*	34 (89)	31 (86)
Failed therapy		
Death during treatment, *n (%)*	1 (2.5)	2 (5.5)
Active infection at 14 days, *n (%)*	3 (8)	2 (5.5)
Positive blood cultures 2 days after the end of treatment, *n*	0	0
Relapse, *n (%)*	0	1 (3)
Outcome during treatment		
Mean duration of fever ± SD, *d*	4.2 ± 4.0	3.7 ± 3.4
New pulmonary emboli, *n (%)*	6 (16)	4 (11)
Renal failure, *n (%)*	3 (8)	5 (14)
Positive blood cultures at 4 days, *n (%)*	1 (2.5)	0

* $P > 0.2$ for all comparisons.

L1-1752

Influence of Empiric Therapy with a β-Lactam Alone or Combined with an Aminoglycoside on Prognosis of Bacteremia Due to Methicillin-Susceptible *Staphylococcus aureus* (MSSA)

L. MORATA, A. SORIANO, J. MARTINEZ, N. COBOS-TRIGUEROS, Z. SANTOS, M. CHAVES, H. STERZIK, M. ALMELA, C. PITART, F. MARCO, J. MENSA;

Hosp. Clinic-IDIBAPS, Barcelona, Spain.

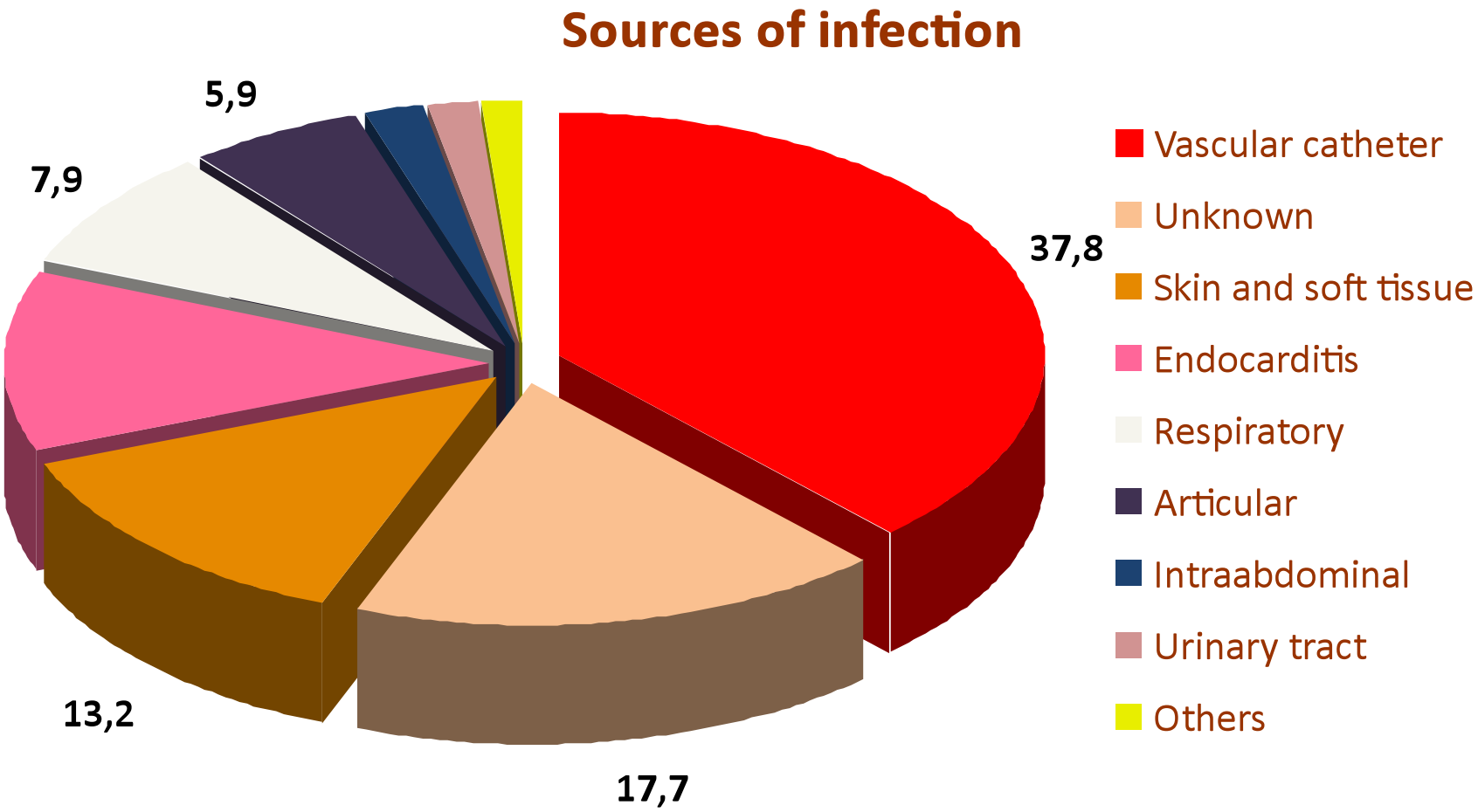
L1-1752

Influence of Empiric Therapy with a β-Lactam Alone or Combined with an Aminoglycoside on Prognosis of Bacteremia Due to Methicillin-Susceptible *Staphylococcus aureus* (MSSA)

- Estudio retrospectivo entre 1991 y 2008, de 1077 episodios de bacteriemia por MSSA
- Análisis uni y multivariable de mortalidad a los 30 días del trat. betalactamico solo ó en combinación con aminoglucosido

L1-1752

Influence of Empiric Therapy with a β-Lactam Alone or Combined with an Aminoglycoside on Prognosis of Bacteremia Due to Methicillin-Susceptible *Staphylococcus aureus* (MSSA)



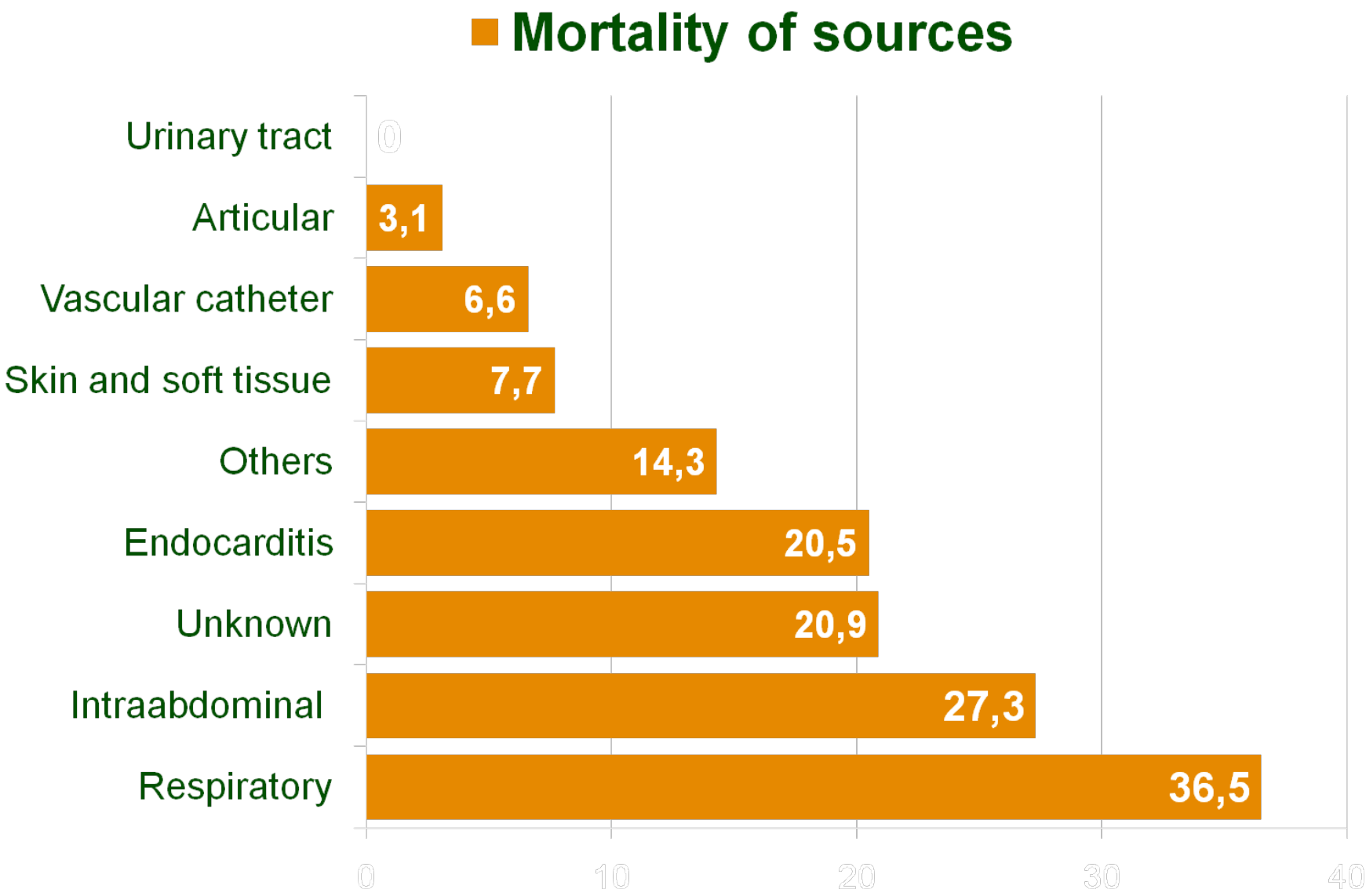
L1-1752

Influence of Empiric Therapy with a β-Lactam Alone or Combined with an Aminoglycoside on Prognosis of Bacteremia Due to Methicillin-Susceptible *Staphylococcus aureus* (MSSA)

- Combinación en 218 pacientes (20%)
  - Mas frecuente en VIH, endocarditis, neutropenia, ventilación mecánica y shock
- No combinación 80%
  - Mas en diabetes, cirrosis, enf. rapidamente fatal, desconocida y con catéter

L1-1752

Influence of Empiric Therapy with a β-Lactam Alone or Combined with an Aminoglycoside on Prognosis of Bacteremia Due to Methicillin-Susceptible *Staphylococcus aureus* (MSSA)



L1-1752

Influence of Empiric Therapy with a β-Lactam Alone or Combined with an Aminoglycoside on Prognosis of Bacteremia Due to Methicillin-Susceptible *Staphylococcus aureus* (MSSA)

- Después del ajuste de las variables mas importantes la combinación con aminoglucosido no fue un factor independiente asociado a la mortalidad a 30 días.
- En un subgrupo con infecciones graves de foco abdominal o pulmonar (107 pacientes) se identifico la combinación con aminoglucosido como factor independiente para disminuir la mortalidad en los 30 días

High Vancomycin MIC and Complicated Methicillin-Susceptible *Staphylococcus aureus* Bacteremia

Jose Maria Aguado, Rafael San-Juan, Antonio Lalueza, Francisca Sanz, Joaquin Rodríguez-Otero, Carmen Gómez-Gonzalez, and Fernando Chaves

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 17, No. 6, June 2011

La CMI a la vancomicina podría ser un factor de mal pronóstico en la bacteriemia por SASM

23% cepas VCM ≥1.5 µg/mL por Etest

	CMI < 1,5 µg/mL N = 76	CMI ≥ 1,5 µg/mL N = 23	*P*
Sepsis grave/shock séptico	14,5 %	21,7 %	NS
Bacteriemia complicada	13,2 %	78,3 %	< 0,0001
Mortalidad 30 días	10,5 %	26,1 %	NS
Atribuible	3,9 %	17,4 %	0,083

Los valores elevados de CMI a la vancomicina fueron la única variable independiente relacionada con el riesgo de bacteriemia complicada (OR 22,9; IC95% 6,7-78,1)

Aguado JM, *et al*. EID 2011: 17: 1099-102

La CMI a la vancomicina podría ser un factor de mal pronóstico en la bacteriemia por SASM

Este fenómeno también afecta a los betalactámicos

	Bacteriemia complicada		
	CMI > 1.5	CMI < 1.5	p
Pacientes tratados inicialmente con glucopéptidos (n = 64)	15/18 (83.3%	8/46 (17.4%)	<0.0001
Pacientes tratados inicialmente con betalactámicos (n = 25)	3/5 (60%)	2/20 (10%)	0.064

Aguado JM, *et al*. EID 2011: 17: 1099-102

MAJOR ARTICLE

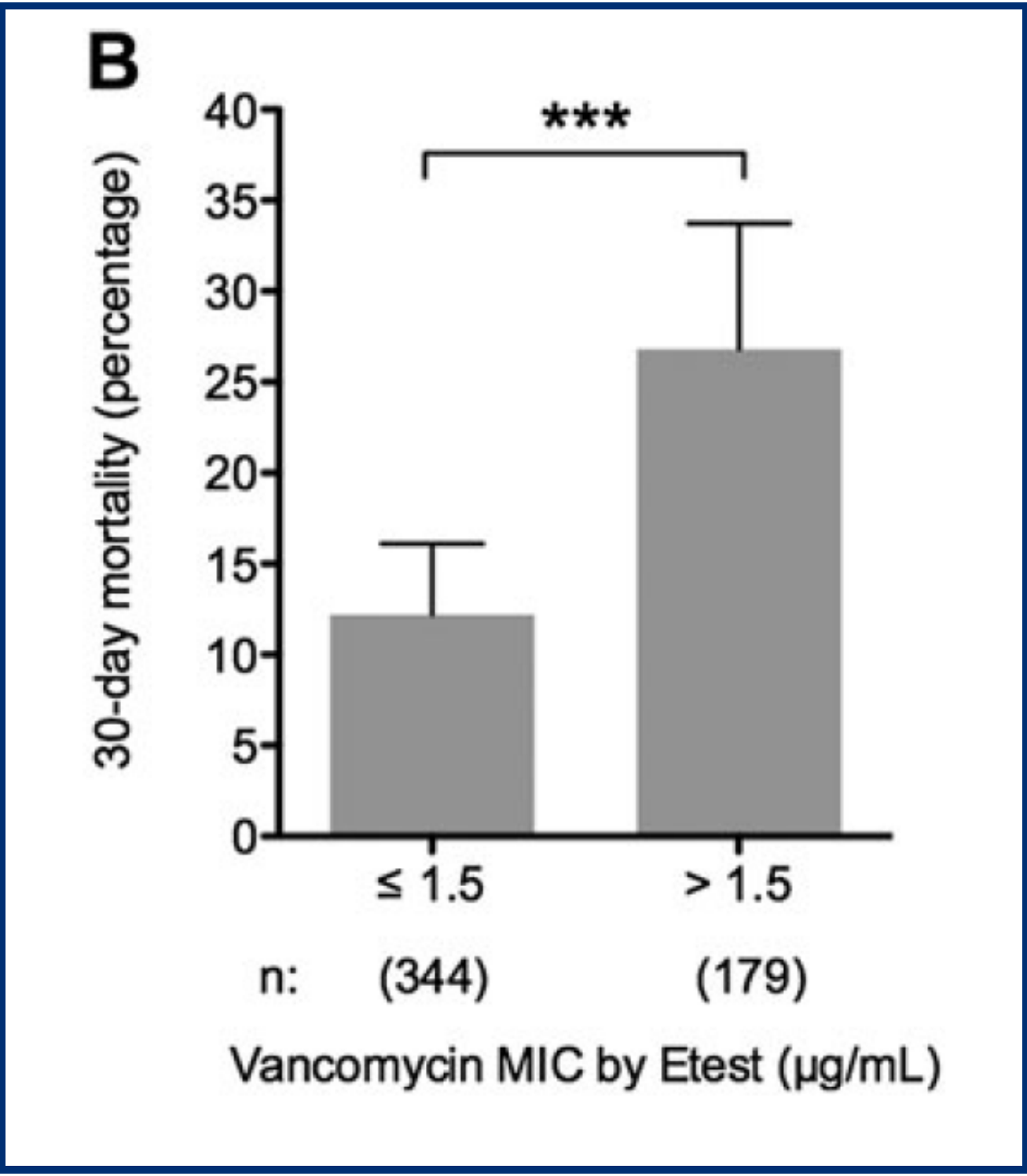
Antibiotic Choice May Not Explain Poorer Outcomes in Patients With *Staphylococcus aureus* Bacteremia and High Vancomycin Minimum Inhibitory Concentrations

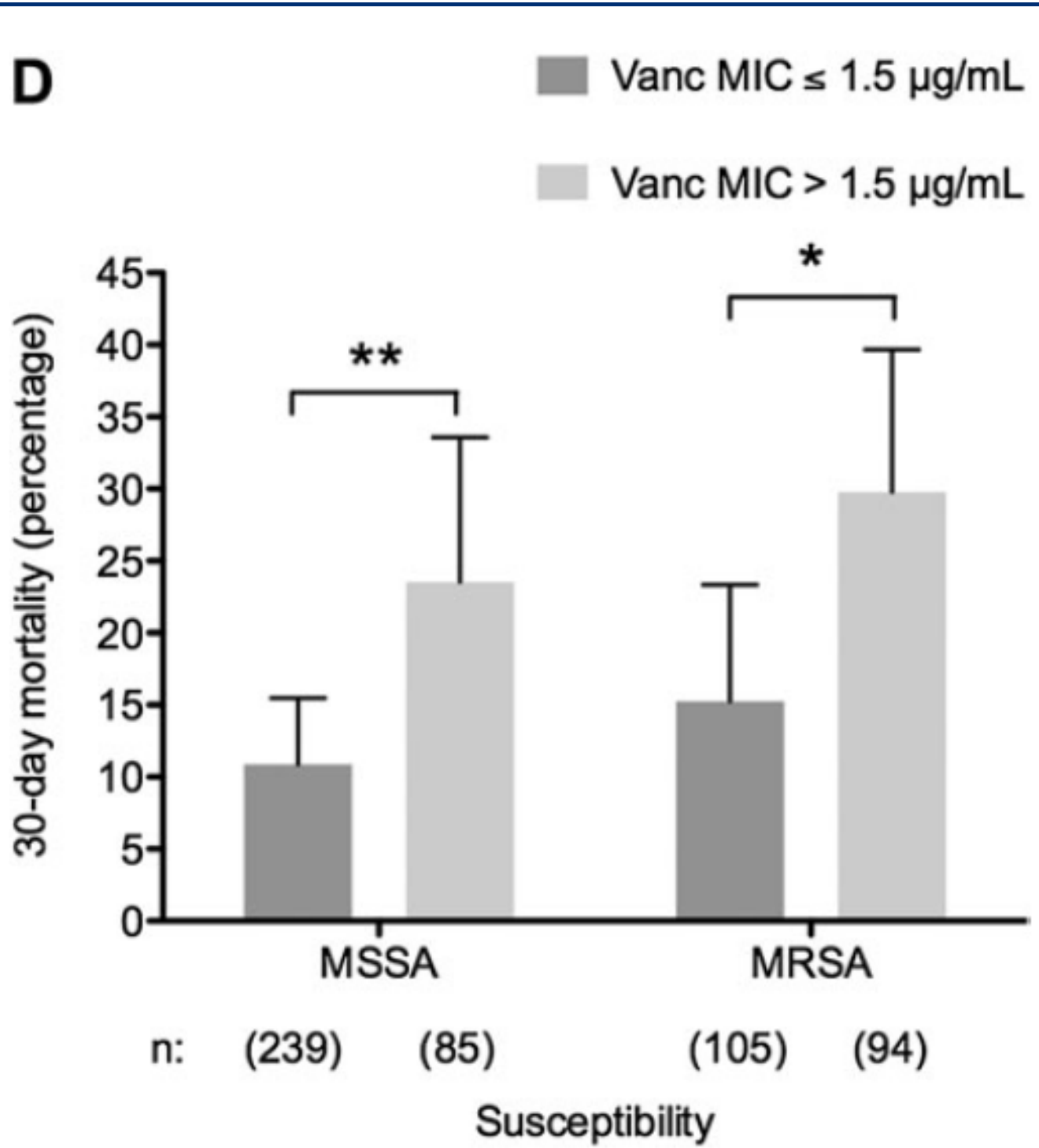
Natasha E. Holmes,[1] John D. Turnidge,[2,3] Wendy J. Munckhof,[4,5] James O. Robinson,[6] Tony M. Korman,[7,8] Matthew V. N. O'Sullivan,[9] Tara L. Anderson,[10,11] Sally A. Roberts,[2] Wei Gao,[12] Keryn J. Christiansen,[13,14] Geoffrey W. Coombs,[13] Paul D. R. Johnson,[1,15,16,a] and Benjamin P. Howden[1,12,15,17,a]

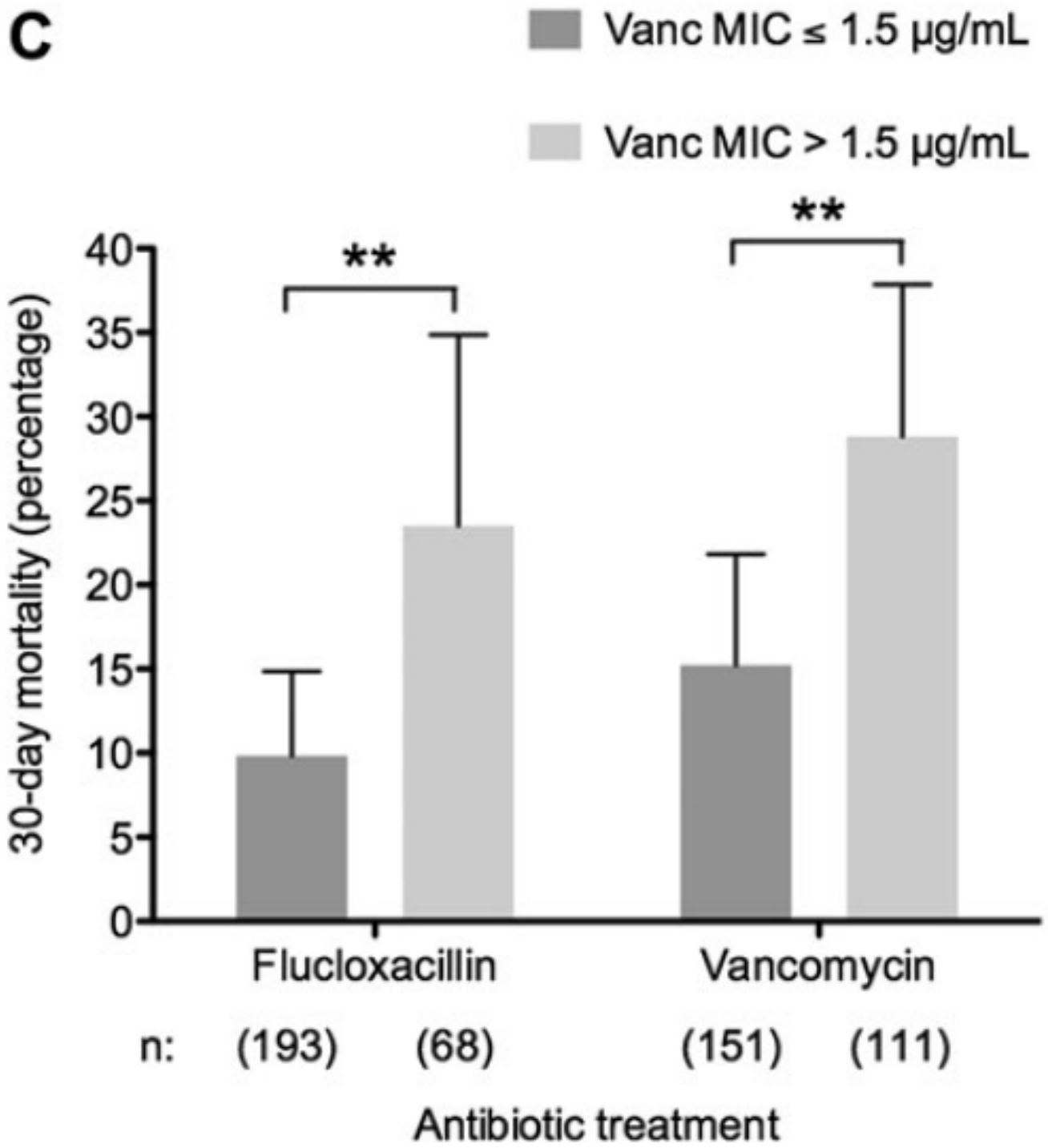
The Journal of Infectious Diseases 2011;204:340–47

532 pacientes con bacteriemia por **S. aureus** recogidas en 8 hospitales entre en 2007-Nov 2008, Cada paciente tratado con vancomicina fue seguido de otro tratado con cloxacilina

26% de SASM CMI>1,5 mg/L (Etest)


B
***
40
35
30
25
20
15
10
5
0
30-day mortality (percentage)
≤ 1.5
> 1.5
n:
(344)
(179)
Vancomycin MIC by Etest (µg/mL)


D
Vanc MIC ≤ 1.5 µg/mL
Vanc MIC > 1.5 µg/mL
30-day mortality (percentage)
45
40
35
30
25
20
15
10
5
0
**
*
MSSA
MRSA
n:
(239)
(85)
(105)
(94)
Susceptibility


C
Vanc MIC ≤ 1.5 µg/mL
Vanc MIC > 1.5 µg/mL
**
**
30-day mortality (percentage)
40
35
30
25
20
15
10
5
0
Flucloxacillin
Vancomycin
n:
(193)
(68)
(151)
(111)
Antibiotic treatment

K-1122

Influence of Vancomycin (VAN) MIC on the Outcome of Cloxacillin-Treated Methicillin-Susceptible *Staphylococcus aureus* (MSSA) Left-Sided Infective Endocarditis (IE)

C. Cervera, MD, PhD - *Physician*, X. Castañeda, MD - *Physician*, A. del Río, MD, PhD - *Physician*, C. García de la María, MD, PhD - *Physician*, D. Soy, MD, PhD - *Physician*, A. Moreno, MD, PhD - *Physician*, C. Falces, MD, PhD - *Physician*, Y. Armero, MD - *Physician*, J. Pericas, MD - *Physician*, M. Almela, MD, PhD - *Physician*, S. Ninot, MD, PhD - *Physician*, J. Pare, MD, PhD - *Physician*, C. Mestres, MD, PhD - *Physician*, J. Gatell, MD, PhD - *Physician*, F. Marco, MD, PhD - *Physician*, J. M. Miro, MD, PhD - *Physician*;

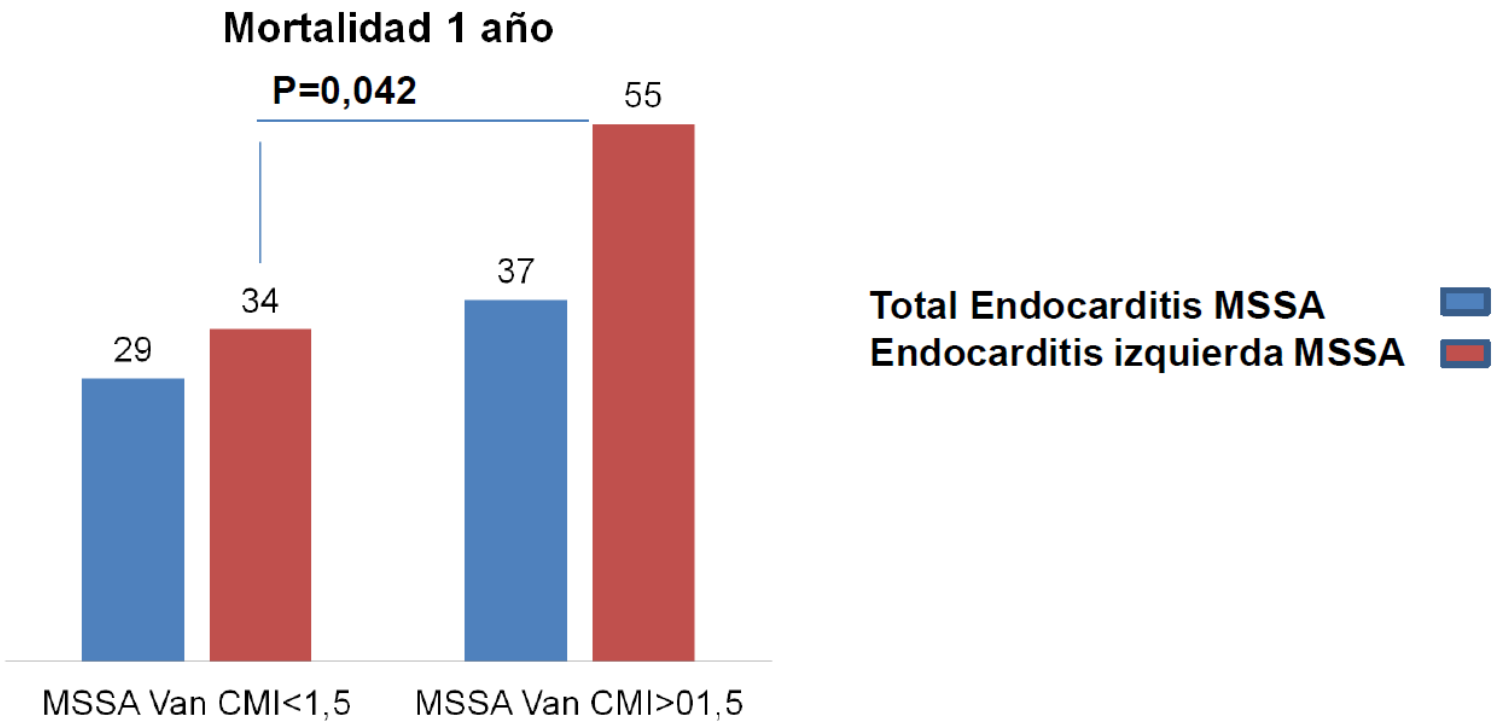
ICAAC 2012

Mortalidad de Pacientes con EI tratados con Cloxacilina y CMI para Vancomicina≥1,5

762 pacientes con Endocarditis infecciosa.

228 EI S. aureus: 137 MSSA (133 tratados con cloxacilina) y 61 MRSA.

Objetivo evaluar asociación entre MSSA CMI Van ≥ 1,5 y mortalidad a un año.



Cervera C et al. ICAAC San Francisco 2012, presentación oral

K-1122

Influence of Vancomycin (VAN) MIC on the Outcome of Cloxacillin-Treated Methicillin-Susceptible *Staphylococcus aureus* (MSSA) Left-Sided Infective Endocarditis (IE)

En análisis de regresión logística la mortalidad de las EI izquierdas por S. aureus con CMI vanco > 1,5 tratadas con cloxacilina, fue un factor independiente de mortalidad después de ajustar por insuficiencia cardiaca, insuficiencia renal, absceso perianular, Charlson, sitio de infección, prótesis y cirugía cardiaca

¿ Que alternativas tenemos?

- 1.- Tratamiento solo con cloxacilina optimizando su administración
- 2.- Buscar nuevas asociaciones
  - Quinolonas
  - Fosfomicina

AAC
Journals.ASM.org

High-Dose Daptomycin plus Fosfomycin Is Safe and Effective in Treating Methicillin-Susceptible and Methicillin-Resistant *Staphylococcus aureus* Endocarditis

José M. Miró,[a] José M. Entenza,[b] Ana del Río,[a] Maria Velasco,[c] Ximena Castañeda,[a] Cristina Garcia de la Mària,[a] Marlyse Giddey,[b] Yolanda Armero,[a] Juan M. Pericàs,[a] Carlos Cervera,[a] Carlos A. Mestres,[a] Manuel Almela,[a] Carlos Falces,[a] Francesc Marco,[a] Philippe Moreillon,[b] Asuncion Moreno,[a] and the Hospital Clinic Experimental Endocarditis Study Group

Hospital Clínic—IDIBAPS, University of Barcelona, Barcelona, Spain[a]; Department of Fundamental Microbiology, University of Lausanne, Lausanne, Switzerland[b]; and Hospital Universitario Fundación Alcorcón, Madrid, Spain[c]

We describe 3 patients with left-sided staphylococcal endocarditis (1 with methicillin-susceptible *Staphylococcus aureus* [MSSA] prosthetic aortic valve endocarditis and 2 with methicillin-resistant *S. aureus* [MRSA] native-valve endocarditis) who were successfully treated with high-dose intravenous daptomycin (10 mg/kg/day) plus fosfomycin (2 g every 6 h) for 6 weeks. This combination was tested *in vitro* against 7 MSSA, 5 MRSA, and 2 intermediately glycopeptide-resistant *S. aureus* isolates and proved to be synergistic against 11 (79%) strains and bactericidal against 8 (57%) strains. This combination deserves further clinical study.

¿ Que alternativas tenemos?

- 1.- Tratamiento solo con cloxacilina optimizando su administración

- 2.- Buscar nuevas asociaciones
  - Quinolonas
  - Fosfomicina
  - Daptomicina

β-Lactams Increase the Antibacterial Activity of Daptomycin against Clinical Methicillin-Resistant *Staphylococcus aureus* Strains and Prevent Selection of Daptomycin-Resistant Derivatives

Shrenik Mehta, Christopher Singh, Konrad B. Plata, Palas K. Chanda, Arundhati Paul, Sarah Riosa, Roberto R. Rosato, and Adriana E. Rosato

Antimicrobial Agents and Chemotherapy p. 6192–6200 December 2012 Volume 56 Number 12

Use of Antistaphylococcal β-Lactams to Increase Daptomycin Activity in Eradicating Persistent Bacteremia Due to Methicillin-Resistant *Staphylococcus aureus*: Role of Enhanced Daptomycin Binding

Abhay Dhand,[1] Arnold S. Bayer,[3,4] Joseph Pogliano,[5] Soo-Jin Yang,[3,4] Michael Bolaris,[3] Victor Nizet,[5] Guiquing Wang,[2] and George Sakoulas[1,5,6]

Clinical Infectious Diseases 2011;53(2):158–163

Guía de tratamiento antimicrobiano de la infección por *Staphylococcus aureus*

José Mensa[1]
Alex Soriano[1]
Pedro Llinares[2]
José Barberán[3]
Miguel Montejo[4]
Miguel Salavert[5]
Luís Alvarez-Rocha[2]
Emilio Maseda[6]
Alfonso Moreno[7]
Juan Pasquau[8]
Joaquín Gómez[9]
Jorge Parra[10]
Javier Candel[11]
José Ramón Azanza[12]
José Elías García[13]
Francesc Marco[1]
Dolores Soy[1]
Santiago Grau[14]
Javier Arias[11]
Jesus Fortún[15]
Cesar Aristides de Alarcón[16]
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Sociedad Española de Quimioterapia (SEQ)
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[1]Hospital Clinic, Barcelona
[2]Complejo Hospitalario de La Coruña
[3]Hospital Universitario Monteprincipe, Madrid
[4]Hospital de Cruces, Bilbao
[5]Hospital La Fe, Valencia
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[7]Hospital Central de Asturias, Oviedo
[8]Hospital Virgen de Las Nieves, Granada
[9]Hospital Virgen de la Arrixaca, Murcia
[10]Hospital Clínico San Cecilio, Granada
[11]Hospital Clínico San Carlos, Madrid
[12]Clínica Universitaria de Navarra, Pamplona
[13]Hospital Universitario de Salamanca, Salamanca
[14]Hospital Del Mar, Barcelona
[15]Hospital Ramón y Cajal, Madrid
[16]Hospital Virgen del Rocio, Sevilla

Localización	SASM[1]
Endocarditis[6]	
Válvula nativa	Cloxacilina ± gentamicina[7] (3-5 días)

- En la infección por SASM con CMI de vancomicina >1 mg/L, criterios de sepsis grave o bacteriemia >5-7 días, considerar la adición de daptomicina.

ORIGINALES

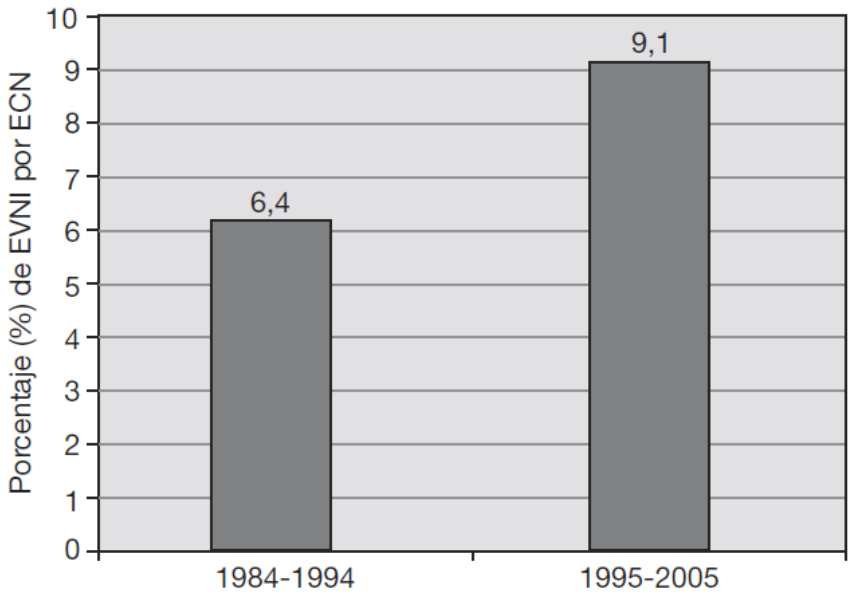
Endocarditis en válvulas nativas izquierdas por estafilococos coagulasa negativos: una entidad en alza

Juan Luis Haro[a], José M.ª Lomas[b], Antonio Plata[c], Josefa Ruiz[d], Juan Gálvez[e], Javier de la Torre[f], Carmen Hidalgo-Tenorio[g], José M.ª Reguera[c], Manuel Márquez[d], Francisco Martínez-Marcos[b] y Arístides de Alarcón[a] por el Grupo para el Estudio de las Infecciones Cardiovasculares de la Sociedad Andaluza de Enfermedades Infecciosas

Enferm Infecc Microbiol Clin 2008;26(5):263-8

TABLA 1. **Gérmenes causantes de endocarditis sobre válvula nativa izquierda**

Patógeno	Número	Porcentaje
Streptococcus grupo viridans	113	24
Staphylococcus aureus	103	21,9
Enterococos	52	10,9
Otros estreptococos	48	10,2
Estafilococos coagulasa negativos	39	8,3
Polimicrobiana	18	4
Bacilos gramnegativos	12	2,6
Coxiella burnetti	10	2,1
Brucella spp.	9	1,9
Hongos	5	1,1
Grupo HACEK	5	1,1
Otros	12	2,6
No filiada	44	9,3
Total	***470***	***100***



Con respecto al tratamiento, todos los pacientes recibieron antibioterapia, con una mediana de 28 días (RIQ: 26-42). La pauta más frecuente fue la asociación de cloxacilina o vancomicina con un aminoglucósido (14 pacientes, 35,9%), seguida de la monoterapia con cloxacilina o vancomicina (13 pacientes, 33,3%) y de la combinación con cloxacilina o vancomicina más aminoglucósido y rifampicina (7 pacientes, 18%).

MAJOR ARTICLE

CID 2008:46

Emergence of Coagulase-Negative Staphylococci as a Cause of Native Valve Endocarditis

Vivian H. Chu,[1,2] Christopher W. Woods,[1,3] Jose M. Miro,[5] Bruno Hoen,[7] Christopher H. Cabell,[1,2] Paul. A. Pappas,[2] Jerome Federspiel,[1] Eugene Athan,[9] Martin E. Stryjewski,[2,11] Francisco Nacinovich,[12] Francesc Marco,[5] Donald P. Levine,[4] Tom S. Elliott,[13] Claudio Q. Fortes,[14] Pilar Tornos,[6] David L. Gordon,[10] Riccardo Utili,[15] Francois Delahaye,[8] G. Ralph Corey,[1,2] and Vance G. Fowler, Jr.,[1,2] for the International Collaboration on Endocarditis–Prospective Cohort Study Group[a]

Patients with CoNS native valve endocarditis	
Community acquired (n = 65)	Health care associated[a] (n = 63)

EI protésica por **Staphylococcus sp**

Recomendaciones combinación antibióticos en EI protésicas estafilococicas

Estudios in vitro

- Saginur R et al. *A A C* 2006
- Monzon Met al. *JAC* 2001

Modelo animal

- Vazquez GJ et al. *AAC* 1980
- Archer GL et al. *JAMA* 1978
- Kobasa WD *Rev Infect Dis* 1983

Combinación antibióticos en EI protésicas estafilococicas. Estudios clínicos

Drinkovic D et al. JAC 2003

- En análisis retrospectivo de pacientes con PVE estafilococica tratados en combinación el cultivo de la válvula de pacientes operados fue 5,9 veces mas negativo que en los tratados con monoterapia

Karchmer AW et al. An Intern Med 1983

- Un estudio observacional de 75 pacientes con PVE por S. epidermidis encontró que la combinación de rifampicina o un aminoglucosido con vancomicina se asocio con mejor pronostico que los tratados con monoterapia
- 81% vs 50% (p = 0,06)

Coagulase-negative staphylococcal prosthetic valve endocarditis—a contemporary update based on the International Collaboration on Endocarditis: prospective cohort study

V H Chu,[1,2] J M Miro,[3] B Hoen,[4] C H Cabell,[1,2] P A Pappas,[2] P Jones,[5] M E Stryjewski,[2,6] I Anguera,[7] S Braun,[8] P Muñoz,[9] P Commerford,[10] P Tornos,[11] J Francis,[12] M Oyonarte,[13] C Selton-Suty,[14] A J Morris,[15] G Habib,[16] B Almirante,[11] D J Sexton,[1] G R Corey,[1,2] V G Fowler Jr,[1,2] for the International Collaboration on Endocarditis-Prospective Cohort Study Group

Heart 2009;**95**:570–576.

Table 4 Antibiotics received by patients with coagulase-negative staphylococcal prosthetic valve endocarditis

Antibiotic regimen	No of patients	In-hospital death (%)
Vancomycin only	15	4 (27)
+ rifampin	12	4 (33)
+ aminoglycoside	15	3 (20)
+ rifampin and aminoglycoside	16	3 (19)
Vancomycin total	58	14 (23)
Penicillinase-resistant penicillin only	5	1 (20)
+ rifampin	1	0
+ aminoglycoside	3	0
+ rifampin and aminoglycoside	6	3 (50)
Penicillinase-resistant penicillin total	15	4 (27)
Both vancomycin and penicillinase-resistant penicillin	4	0
Other*	9	3 (33)

*Other regimens included combinations of the following antibiotics: aminoglycosides, rifampin, daptomycin, teicoplanin, levofloxacin, dicloxacillin and augmentin.

Is triple theraphy necessary in staphylococcal prosthetic valve endocarditis?

Dr Antonio Plata (1), Dr. Emilio Garcia-Cabrera (2), Dr. Juan Diego Ruiz-Mesa (1), Dr Jose Maria Reguera (1), Dr Jose M Lomas-Cabeza (3), Dr Francisco Martinez-Marcos (3), Dr Javier de la Torre Lima (4), Dra. Josefa Ruiz (5), Dr Juan Galvez-Acebal (6), Dra. Radka Ivanova (5), Dra. Carmen Hidalgo- Tenorio (7), Dr. Aristides de Alarcon (2)

[1]HRU Carlos Haya (Málaga), [2]H. Virgen del Rocío (Sevilla), [3]H. Juan Ramón Jiménez (Huelva), [4]H. Costa del Sol (Marbella), [5]H. Virgen de la Victoria (Málaga), [6]H. Virgen Macarena (Sevilla), [7]H. Virgen de las Nieves (Granada),

Andalusian Group for the Study of Cardiovascular Infection

12th INTERNATIONAL SYMPOSIUM on MODERN CONCEPTS in ENDOCARDITIS and VASCULAR INFECTIONS

GLOBAL CARACTERISTICS

1240 Left sided endocarditis

↓

270 Prostetic Valve endocarditis

↓

109 staphylococcal valve endocarditis

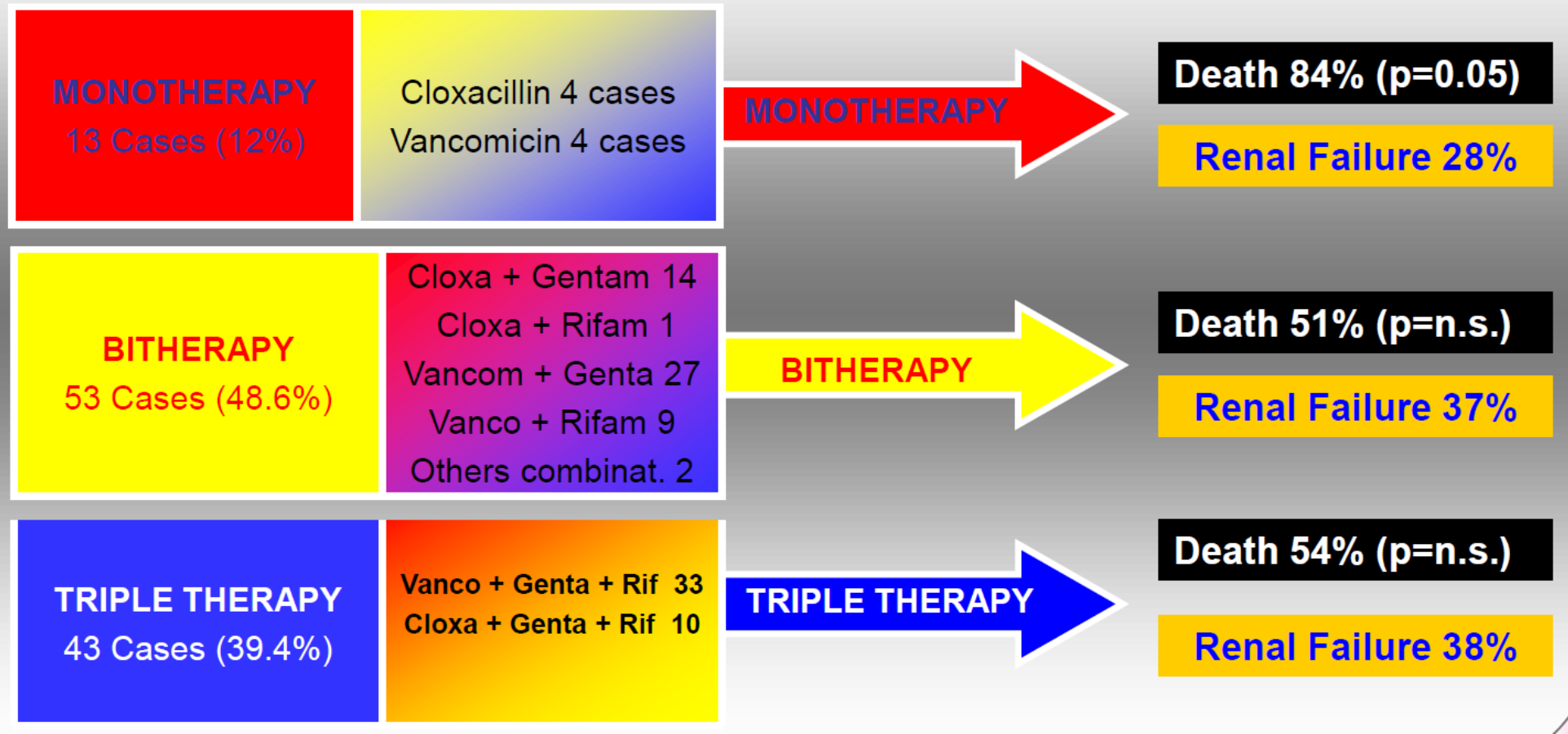
↙ ↘

29 S. aureus (5% MRSA)

80 S. coagulase negative (73% Meticillin Resistant)

Mean Age:	59.4±13.2
Sex	♂ 65.8% ♀ 34.2%
Early prosthetic endocarditis	57 (52.2%)
Late prosthetic endocarditis	52 (47.7%)
Nosocomial	70 (64.2%)
Community	37 (29.4%)
Health care asoociated	2 (1.8%)

MONOTHERAPY / BITHERAPY/ TRIPLE THERAPY



MORTALITY ANALYSIS

UNIVARIATE ANALYSIS

Septic shock	p=0.03
Monotherapy	p=0.046
Surgery delayed	p=0.03
Acute renal failure	p=0.05
Charlson age adjusted	p=0.05
Euroscore	P=0.002
Log Euroscore	P=0.0001

MULTIVARIATE ANALYSIS

Monotherapy	p=0.038	6.8 (IC 95% 1.1-41,5)
Log Euroscore	p=0.0001	1.07 (IC 95% 1.04-1.108)

CONCLUSIONS

✓ All the clinical guidelines recommended triple therapy for staphylococcal prosthetic valve endocarditis (vancomicin/cloxacillin + Gentamicin + Rifampicin) but there aren´t studies that respond clearly this question. In this large serie we found that bitherapy was similar to triple therapy in mortality with similar rates of acute renal failure and probably with less drugs interactions.

✓Monotherapy would not be used in staphylococcal prosthetic valve endocarditis because it has more mortality than bitherapy and triple therapy

CONCLUSIONES 1

- En la EI por streptococcus sp y staphylococcus sp la asociación al betalactamico de un aminoglucosido no parece claramente justificada, especialmente en pacientes mayores y/o con riesgo de Insuficiencia renal. Valoración individual riesgo-beneficio

- En la EI enterococica la asociación ampicilina ceftriaxona debe desplazar a la pauta de ampicilina/penicilina + aminoglucosido

CONCLUSIONES 2

- En el paciente con EI protésica por stahylococcus sp tampoco esta clara la triple terapia
- En EI por streptococcus sp hay pocas alternativas a la asociación a betalactamicos
- En la EI por s. aureus meti S, especialmente si CMI vanco es >1,5, considerar asociar: daptomicina, fosfomicina


IRIS
ESPAÑA

¿Alguna duda?

Severity of Gentamicin's Nephrotoxic Effect on Patients with Infective Endocarditis: A Prospective Observational Cohort Study of 373 Patients

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Clinical Infectious Diseases 2009; 48:65–71

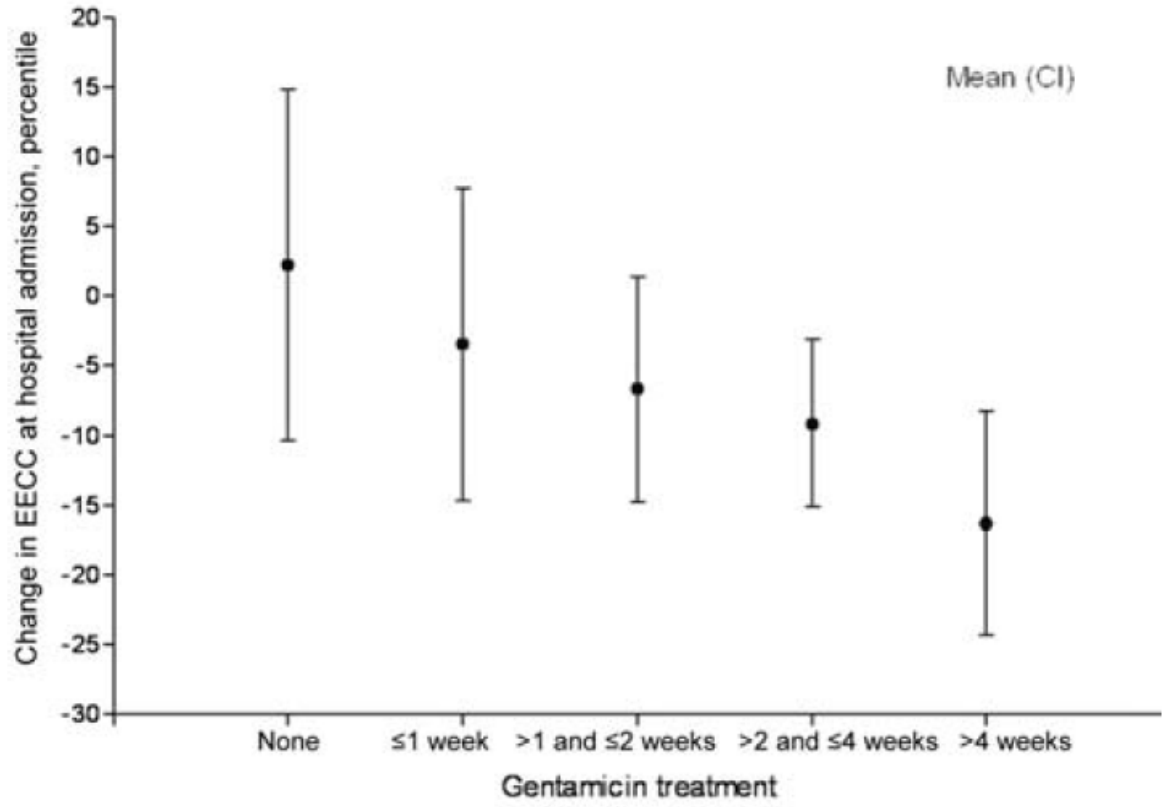


Figure 1. Mean percentile change in endogenous creatinine clearance (EECC) from diagnosis to hospital discharge in 286 patients with infective endocarditis, grouped by days of gentamicin treatment.

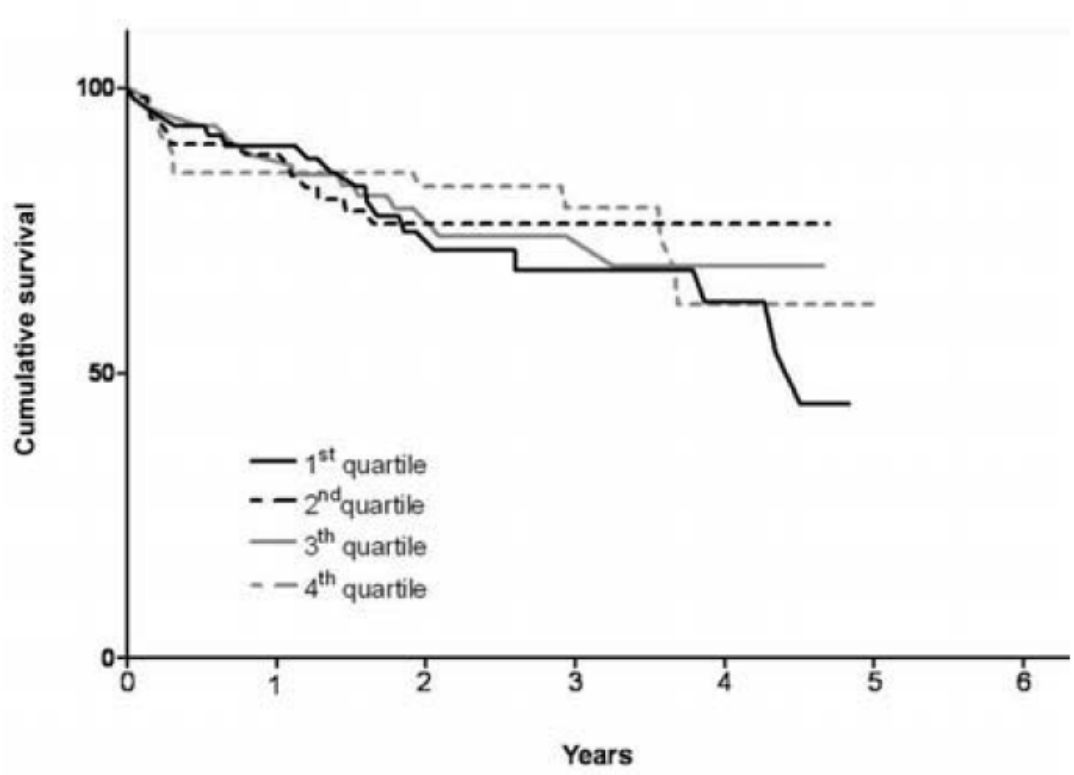


Figure 2. Kaplan-Meier plot of cumulative survival after hospital discharge for 241 patients with infective endocarditis, by percentage change in endogenous creatinine clearance (EECC) from diagnosis to hospital discharge. Patients are divided into quartiles, with EECC quartile intervals as follows: 1st, >7.3%; 2nd, between 7.3% and −11%; 3rd, between −11.3% and −21%; and 4th, less than −21%.

Table 4. Multivariate analysis of change in estimated endogenous creatinine clearance (EECC) between hospital admission and discharge in 286 patients with infective endocarditits (IE), by percentage decrease in EECC.

Variable	Change in EECC ≤10% (n = 142)	Change in EECC >10% (n = 144)	P[a]
Age, mean years ± SD	58.6 ± 16.0	63.3 ± 14.2	.015
Sex			.193
Male	106 (75)	98 (68)	
Female	36 (25)	46 (32)	
Surgery	78 (55)	80 (56)	.166
Diabetes type 1 and 2	10 (7)	9 (6)	
Stroke	19 (13)	18 (13)	
Prosthetic valve pre-IE	30 (21)	41 (28)	.157
Gentamicin groups			.012
No gentamicin	27 (19)	18 (13)	
<1 week	34 (24)	27 (19)	
1–2 weeks	32 (23)	24 (17)	
2–4 weeks	34 (24)	42 (29)	
>4 weeks	17 (12)	31 (22)	

In summary, this study finds a progressive nephrotoxic effect of gentamicin in relation to treatment duration. Even though baseline renal function is an independent prognostic marker of mortality, we found no association between mortality and a gentamicin-induced decrease in renal function during hospitalization to treat IE. Our study does not support the abolishment of AG in treatment of IE.

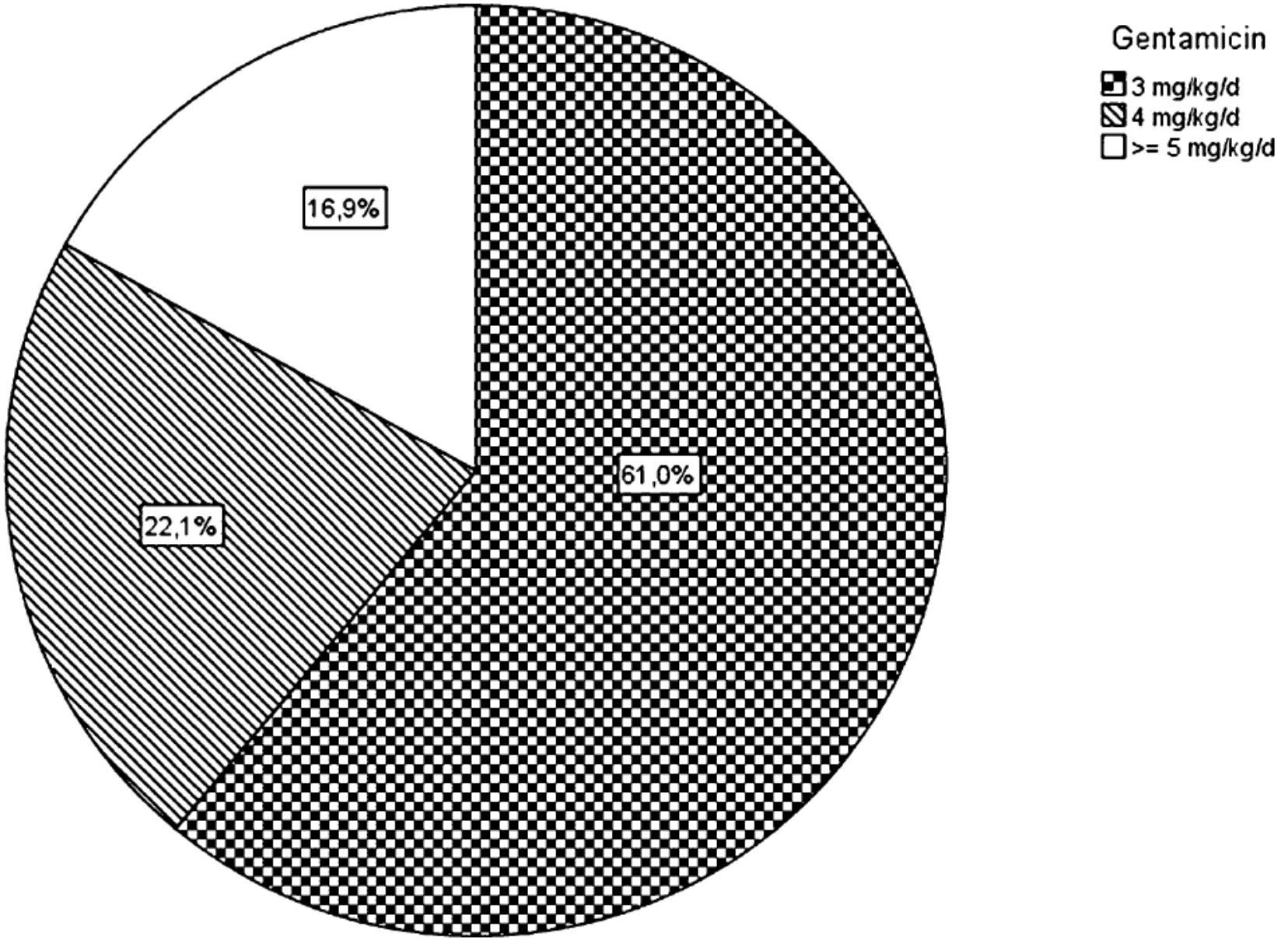
Eur J Clin Microbiol Infect Dis (2012) 31:1413–1418
DOI 10.1007/s10096-011-1458-9

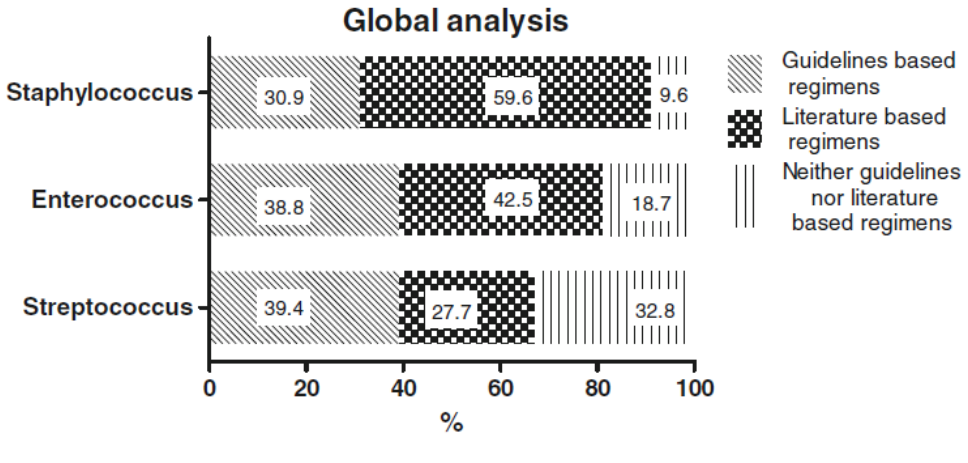
ARTICLE

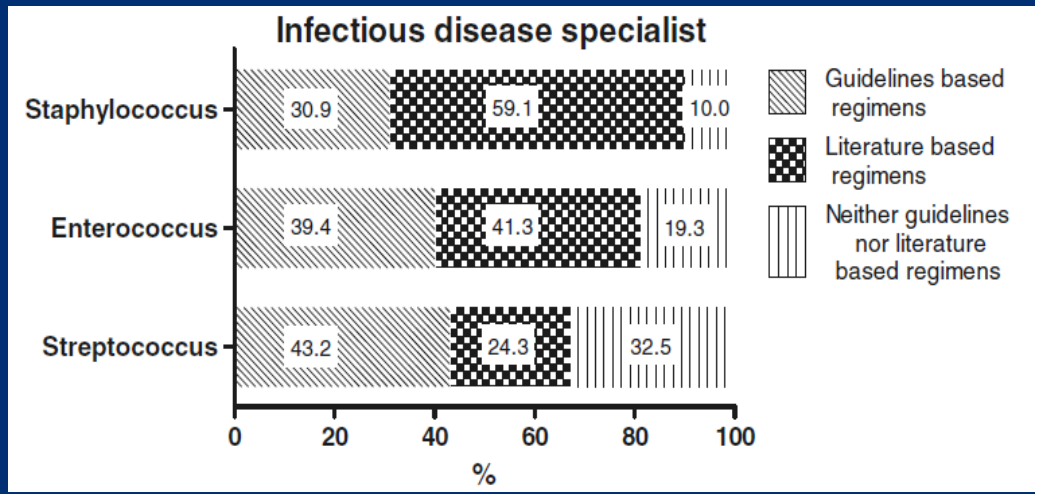
A survey on the use of gentamicin in infective endocarditis

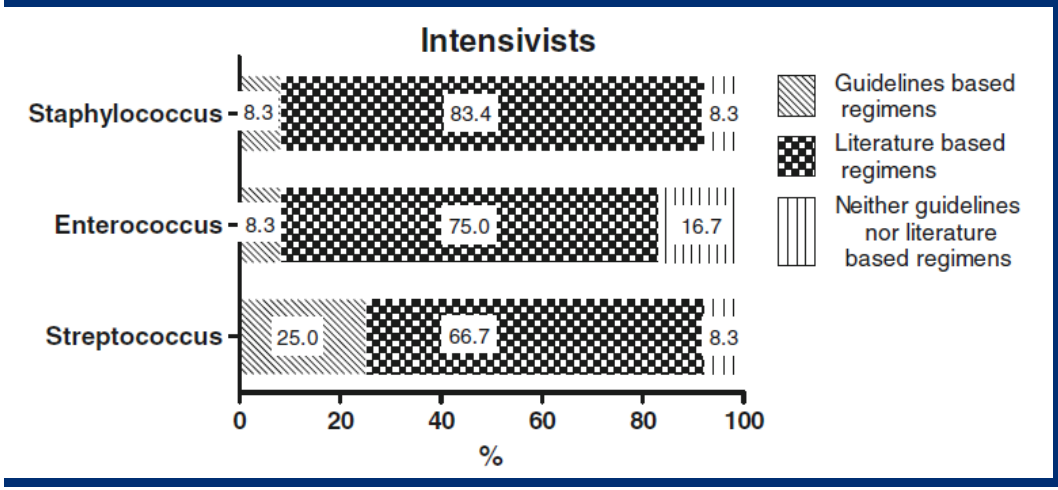
G. Béraud · G. Le Moal · A. Elsendoorn · P. Tattevin · C. Godet · S. Alfandari · W. Couet · P. Roblot · F. Roblot

Which dose of gentamicin do you use in a patient with endocarditis and normal renal function?




Global analysis
Staphylococcus
Enterococcus
Streptococcus
30.9
59.6
9.6
38.8
42.5
18.7
39.4
27.7
32.8
0
20
40
60
80
100
%
Guidelines based regimens
Literature based regimens
Neither guidelines nor literature based regimens


Infectious disease specialist
Staphylococcus
Enterococcus
Streptococcus
30.9
59.1
10.0
39.4
41.3
19.3
43.2
24.3
32.5
0
20
40
60
80
100
%
Guidelines based regimens
Literature based regimens
Neither guidelines nor literature based regimens


Intensivists
Staphylococcus
Enterococcus
Streptococcus
8.3
83.4
8.3
8.3
75.0
16.7
25.0
66.7
8.3
0
20
40
60
80
100
%
Guidelines based regimens
Literature based regimens
Neither guidelines nor literature based regimens

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Consensus document on controversial issues in the diagnosis and treatment of bloodstream infections and endocarditis

Evangelo Boumis [a,*], Giovanni Gesu [b], Francesco Menichetti [c], Marco Ranieri [d], Mauro Rinaldi [e], Fredy Suter [f], Emanuele Nicastri [a,i], Francesco N. Lauria [a,i], Giampiero Carosi [g,i], Mauro Moroni [h,i], Giuseppe Ippolito [a,i],

and the GISIG (Gruppo Italiano di Studio sulle Infezioni Gravi) Working Group on Bloodstream Infections and Endocarditis [1]

Recommendations

In the treatment of native valve MSSA infectious endocarditis, there is no convincing evidence of the usefulness of a combination of gentamicin with either vancomycin or an anti-staphylococcal penicillin, while there is evidence that this combination is associated with an increase in toxicity, especially in patients aged over 65 years. Gentamicin in this condition must therefore be used with caution (B). In the treatment of native valve IE caused by MRSA there is limited evidence on the utility of combination therapy (D). The use of combination therapy is still indicated in the treatment of prosthetic valve *S. aureus* endocarditis (D).