novedades en el tratamiento antimicrobiano

nuria fernández hidalgo
servei de malalties infeccioses
hospital universitari vall d'hebron

introducción

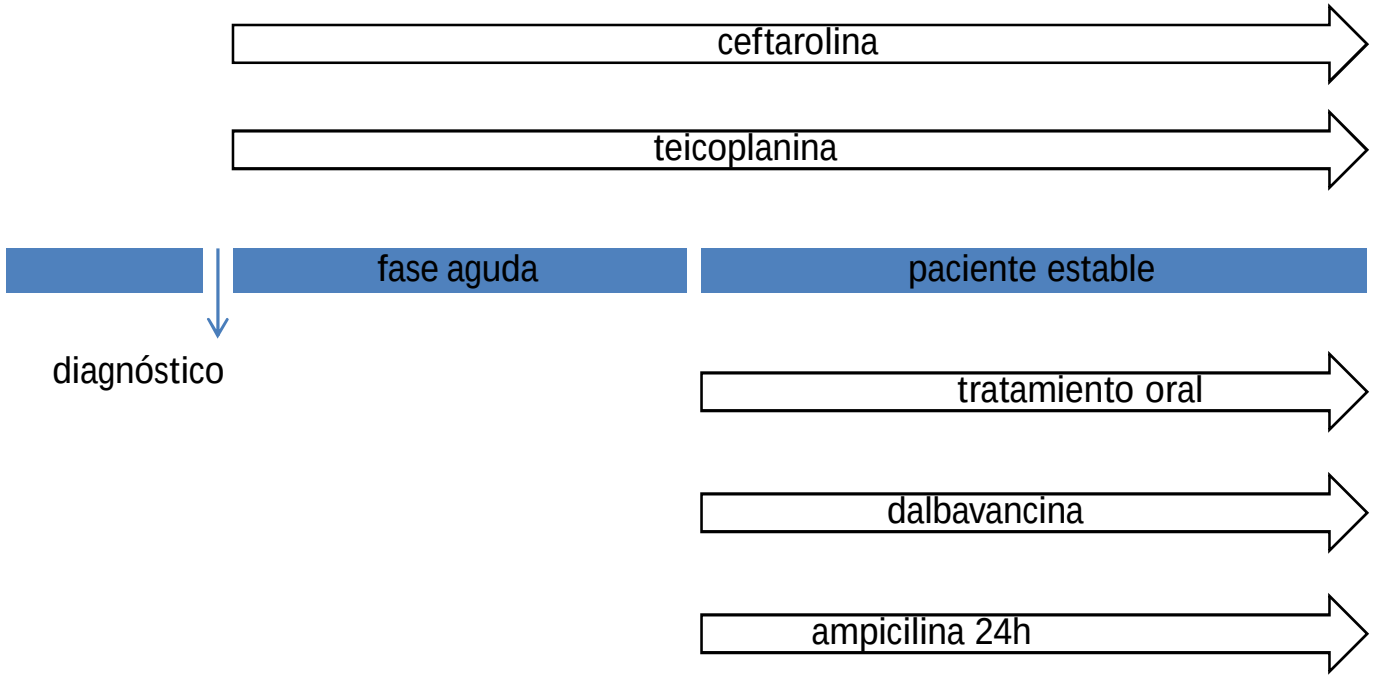
novedad

cosa nueva

artículo de moda

extrañeza o *admiración* que causa lo antes no visto ni oído

índice


ceftarolina
teicoplanina
fase aguda
paciente estable
diagnóstico
tratamiento oral
dalbavancina
ampicilina 24h

fuentes de información

publicaciones

experiencia/s

ENCUESTA SEICAV 2018 "Novedades en el tratamiento antimicrobiano"

Nombre del hospital: _____

CEFTAROLINA

¿Has tratado endocarditis con ceftarolina?

En caso afirmativo: ¿cuántos casos?

¿de qué etiologías?

¿como primera elección o como rescate?

¿cuál ha sido la evolución de los pacientes? (curación, muerte, recidiva)

¿algún efecto secundario destacable?

Colaboración GAMES

4318 episodios de EI (2008 – 2017) pertenecientes a 35 hospitales

↓

11 centros respondieron la encuesta

tratamiento antibiótico oral

Partial oral treatment of endocarditis

Kasper Iversen, MD, DMSc,[a] Nis Høst, MD, PhD,[b] Niels Eske Bruun, MD, DMSc,[c] Hanne Elming, MD, PhD,[d] Bettina Pump, MD, DMSc,[d] Jens Jørgen Christensen, MD, DMSc,[e] Sabine Gill, PhD,[f] Flemming Rosenvinge, MD,[g] Henrik Wiggers, MD, DMSc,[h] Kurt Fuursted, MD, DMSc,[i] Claus Holst-Hansen, MD, PhD,[j] Eva Korup, MD, PhD,[j] Henrik Carl Schønheyder, MD, DMSc,[k] Christian Hassager, MD, DMSc,[a] Dan Høfsten, MD, PhD,[a] Jannik Helweg Larsen, MD, DMSc,[l] Claus Moser, MD, PhD,[m] Nikolaj Ihlemann, MD, PhD,[a] and Henning Bundgaard, MD, DMSc[a] *Copenhagen, Roskilde, Slagelse, Odense, Aarhus, and Aalborg, Denmark*

Background Guidelines for the treatment of left-sided infective endocarditis (IE) recommend 4 to 6 weeks of intravenous antibiotics. Conversion from intravenous to oral antibiotics in clinically stabilized patients could reduce the side effects associated with intravenous treatment and shorten the length of hospital stay. Evidence supporting partial oral therapy as an alternative to the routinely recommended continued parenteral therapy is scarce, although observational data suggest that this strategy may be safe and effective.

Study Design This is a noninferiority, multicenter, prospective, randomized, open-label study of partial oral treatment with antibiotics compared with full parenteral treatment in left-sided IE. Stable patients (n = 400) with streptococci, staphylococci, or enterococci infecting the mitral valve or the aortic valve will be included. After a minimum of 10 days of parenteral treatment, stable patients are randomized to oral therapy or unchanged parenteral therapy. Recommendations for oral treatment have been developed based on minimum inhibitory concentrations and pharmacokinetic calculations. Patients will be followed up for 6 months after completion of antibiotic therapy. The primary end point is a composition of all-cause mortality, unplanned cardiac surgery, embolic events, and relapse of positive blood cultures with the primary pathogen.

Conclusion The Partial Oral Treatment of Endocarditis study tests the hypothesis that partial oral antibiotic treatment is as efficient and safe as parenteral therapy in left-sided IE. The trial is justified by a review of the literature, by pharmacokinetic calculations, and by our own experience. (Am Heart J 2013;165:116-22.)

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D., Trine Madsen, M.D., Ph.D., Hanne Elming, M.D., Ph.D., Kaare T. Jensen, M.D., Ph.D., Niels E. Bruun, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc., Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine F. Klein, M.D., Emil L. Fosbøll, M.D., Ph.D., Flemming Rosenvinge, M.D., Henrik C. Schønheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc., Christian Torp-Pedersen, M.D., D.M.Sc., Jannik Helweg-Larsen, M.D., D.M.Sc., Niels Tønder, M.D., D.M.Sc., Claus Moser, M.D., Ph.D., and Henning Bundgaard, M.D., D.M.Sc.

ABSTRACT

BACKGROUND

Patients with infective endocarditis on the left side of the heart are typically treated with intravenous antibiotic agents for up to 6 weeks. Whether a shift from intravenous to oral antibiotics once the patient is in stable condition would result in efficacy and safety similar to those with continued intravenous treatment is unknown.

METHODS

In a randomized, noninferiority, multicenter trial, we assigned 400 adults in stable condition who had endocarditis on the left side of the heart caused by streptococcus, *Enterococcus faecalis*, *Staphylococcus aureus*, or coagulase-negative staphylococci and who were being treated with intravenous antibiotics to continue intravenous treatment (199 patients) or to switch to oral antibiotic treatment (201 patients). In all patients, antibiotic treatment was administered intravenously for at least 10 days. If feasible, patients in the orally treated group were discharged to outpatient treatment. The primary outcome was a composite of all-cause mortality, unplanned cardiac surgery, embolic events, or relapse of bacteremia with the primary pathogen, from the time of randomization until 6 months after antibiotic treatment was completed.

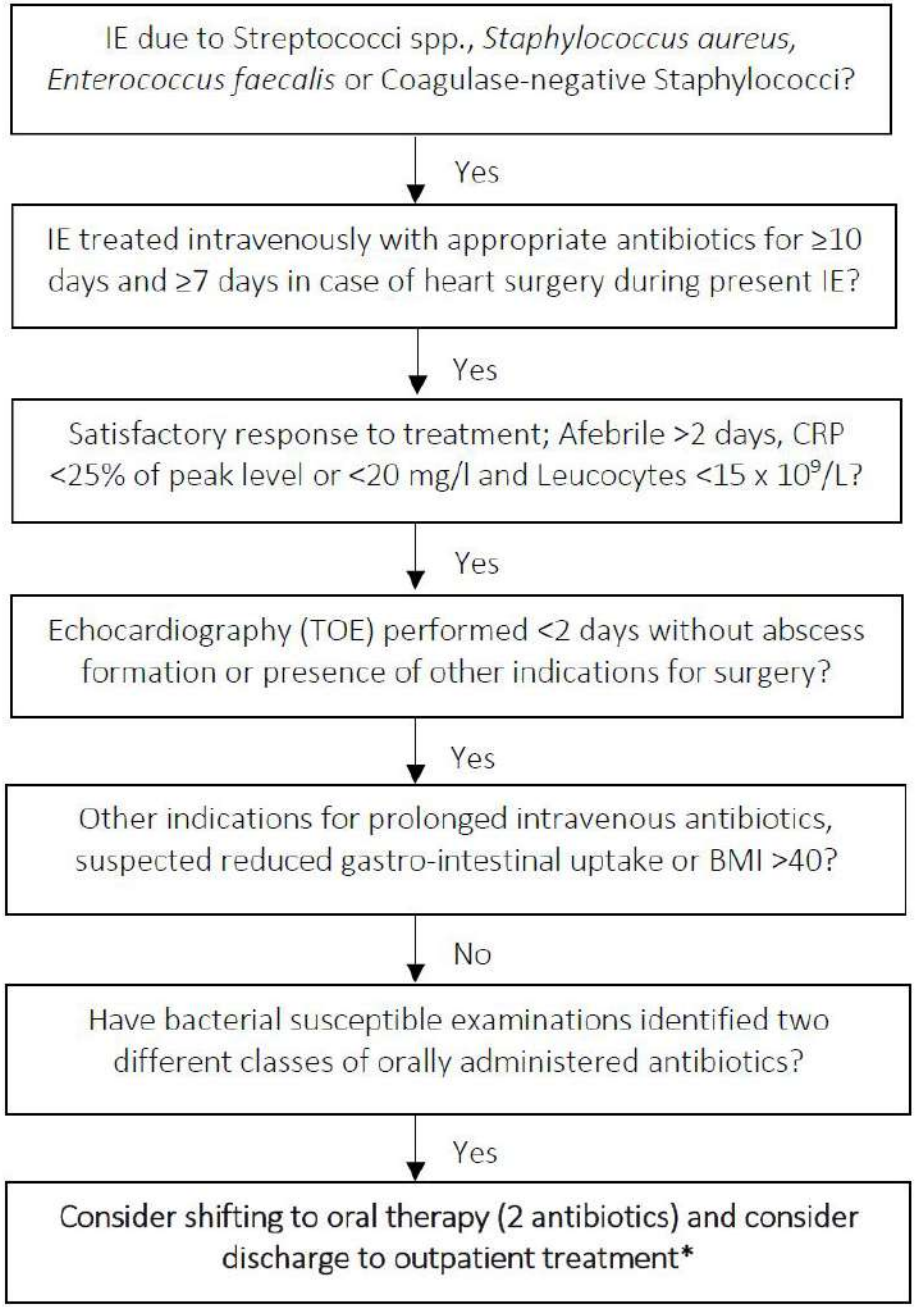
The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Bundgaard at the Department of Cardiology B 2141, the Heart Center, Rigshospitalet, Copenhagen University Hospital, Blegdamsvej 9, 2100 Copenhagen, Denmark, or at henning.bundgaard@regionh.dk.

Drs. Iversen, Ihlemann, Høfsten, Fosbøll, Køber, and Bundgaard are members of Copenhagen Health Science Partners.

This article was published on August 28, 2018, at NEJM.org.

DOI: 10.1056/NEJMoa1808312

Copyright © 2018 Massachusetts Medical Society.


IE due to Streptococci spp., *Staphylococcus aureus*, *Enterococcus faecalis* or Coagulase-negative Staphylococci?
Yes
IE treated intravenously with appropriate antibiotics for ≥10 days and ≥7 days in case of heart surgery during present IE?
Yes
Satisfactory response to treatment; Afebrile >2 days, CRP <25% of peak level or <20 mg/l and Leucocytes <15 x 10^9/L?
Yes
Echocardiography (TOE) performed <2 days without abscess formation or presence of other indications for surgery?
Yes
Other indications for prolonged intravenous antibiotics, suspected reduced gastro-intestinal uptake or BMI >40?
No
Have bacterial susceptible examinations identified two different classes of orally administered antibiotics?
Yes
Consider shifting to oral therapy (2 antibiotics) and consider discharge to outpatient treatment*

Penicillin and methicillin sensitive *Staphylococcus aureus* and coagulase-negative staphylococci:

1) Amoxicillin 1 g x 4 and [redacted]
2) Amoxicillin 1 g x 4 and rifampicin 0.6 g x 2
3) Linezolid 0.6 g x 2 and [redacted]
4) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2

Methicillin sensitive *Staphylococcus aureus* and coagulase-negative staphylococci

1) Dicloxacillin 1 g x 4 and [redacted]
2) Dicloxacillin 1 g x 4 and rifampicin 0.6 g x 2
3) Linezolid 0.6 g x 2 and [redacted]
4) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2

Methicillin resistant coagulase-negative staphylococci

1) Linezolid 0.6 g x 2 and [redacted]
2) Linezolid 0.6 g x 2 and rifampicin 0.6 g x2

Enterococcus faecalis:

1) Amoxicillin 1 g x 4 and rifampicin 0.6 g x 2
2) Amoxicillin 1 g x 4 and moxifloxacin 0.4 g x 1
3) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2
4) Linezolid 0.6 g x 2 and moxifloxacin 0.4 g x 1

Streptococci with a minimal inhibitory concentration for penicillin of <1 mg/L:

1) Amoxicillin 1 g x 4 and rifampicin 0.6 g x 2
2) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2
3) Linezolid 0.6 g x 2 and moxifloxacin 0.4 g x1

Streptococci with a minimal inhibitory concentration for penicillin of ≥1 mg/L:

1) Linezolid 0,6 g x2 and rifampicin 0.6 g x 2
2) Moxifloxacin 0.4 g x 1 and rifampicin 0.6 g x 2
3) Moxifloxacin 0.4 g x 1 and clindamycin 06 g x3

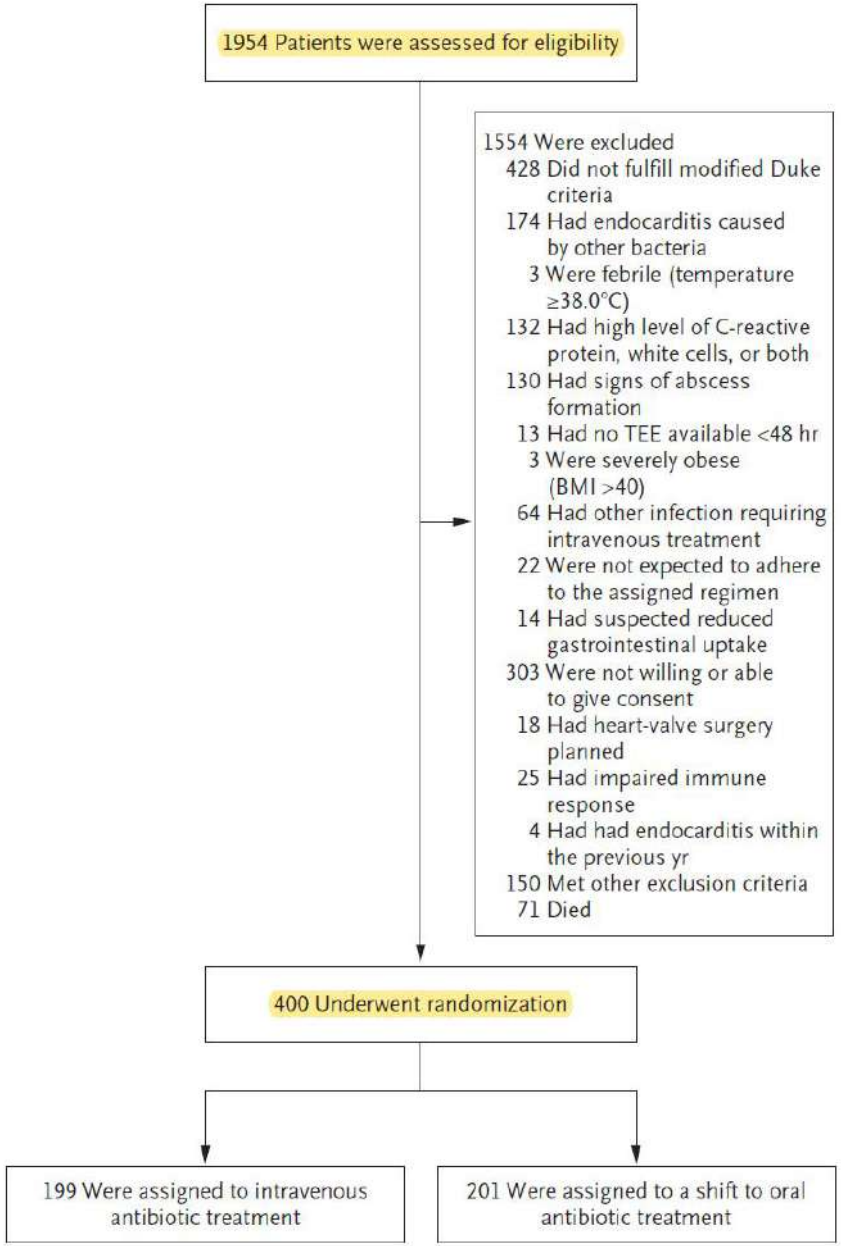

1954 Patients were assessed for eligibility
1554 Were excluded
428 Did not fulfill modified Duke criteria
174 Had endocarditis caused by other bacteria
3 Were febrile (temperature ≥38.0°C)
132 Had high level of C-reactive protein, white cells, or both
130 Had signs of abscess formation
13 Had no TEE available <48 hr
3 Were severely obese (BMI >40)
64 Had other infection requiring intravenous treatment
22 Were not expected to adhere to the assigned regimen
14 Had suspected reduced gastrointestinal uptake
303 Were not willing or able to give consent
18 Had heart-valve surgery planned
25 Had impaired immune response
4 Had had endocarditis within the previous yr
150 Met other exclusion criteria
71 Died
400 Underwent randomization
199 Were assigned to intravenous antibiotic treatment
201 Were assigned to a shift to oral antibiotic treatment

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Intravenous Treatment (N=199)	Oral Treatment (N=201)
Mean age — yr	67.3±12.0	67.6±12.6
Female sex — no. (%)	50 (25.1)	42 (20.9)
Body temperature — °C	36.9±0.45	37.0±0.44
Coexisting condition or risk factor — no. (%)		
Diabetes	36 (18.1)	31 (15.4)
Renal failure	25 (12.6)	21 (10.4)
Dialysis	13 (6.5)	15 (7.5)
COPD	17 (8.5)	9 (4.5)
Liver disease	7 (3.5)	6 (3.0)
Cancer	14 (7.0)	18 (9.0)
Intravenous drug use	3 (1.5)	2 (1.0)
Pathogen — no. (%)†		
Streptococcus	104 (52.3)	92 (45.8)
Enterococcus faecalis	46 (23.1)	51 (25.4)
Staphylococcus aureus‡	40 (20.1)	47 (23.4)
Coagulase-negative staphylococci	10 (5.0)	13 (6.5)

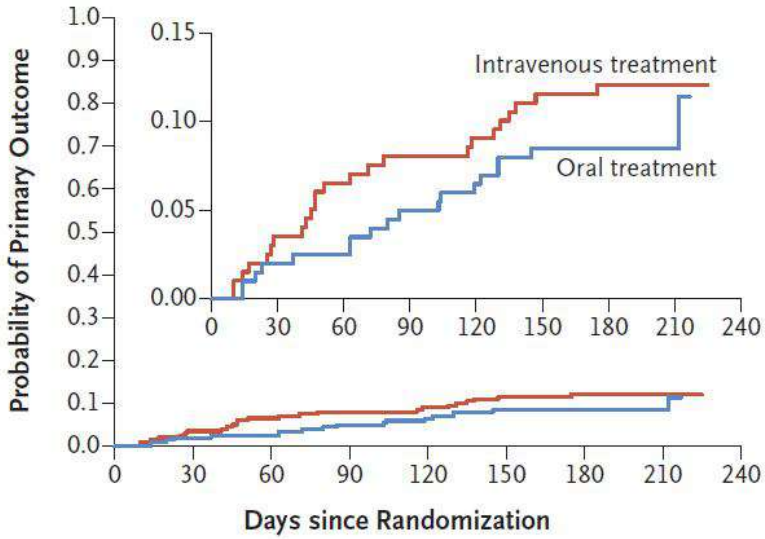
Table 2. Distribution of the Four Components of the Primary Composite Outcome.*

Component	Intravenous Treatment (N=199)	Oral Treatment (N=201)	Difference	Hazard Ratio (95% CI)
	number (percent)		*percentage points (95% CI)*	
All-cause mortality	13 (6.5)	7 (3.5)	3.0 (−1.4 to 7.7)	0.53 (0.21 to 1.32)
Unplanned cardiac surgery	6 (3.0)	6 (3.0)	0 (−3.3 to 3.4)	0.99 (0.32 to 3.07)
Embolic event	3 (1.5)	3 (1.5)	0 (−2.4 to 2.4)	0.97 (0.20 to 4.82)
Relapse of the positive blood culture†	5 (2.5)	5 (2.5)	0 (−3.1 to 3.1)	0.97 (0.28 to 3.33)

* Six patients, three in each group, had two outcomes.
† For details about relapse of the positive blood culture, see the Supplementary Appendix.

composite end-point	12.1%	9.0%	3.1 (-3.4 – 9.6)	p=0.40

	Intravenous treatment	Oral treatment
Causes of death	**12**	**8**
Infection and endocarditis, n (%)	2 (16.7)	2 (25.0)
Infection, not endocarditis, n (%)	2 (16.7)	2 (25.0)
Sudden cardiac death, n (%)	4 (33.3)	0 (0)
Heart failure, n (%)	1 (8.3)	0 (0)
Cerebral haemorrhage, n (%)	1 (8.3)	1 (12.5)
Cancer, n (%)	2 (16.7)	1 (12.5)
Lung disease, (n%)	0 (0)	1 (12.5)
Renal failure, n (%)	0 (0)	1 (12.5)



No. at Risk

Intravenous treatment	199	192	186	183	181	176	174	28	0
Oral treatment	201	197	196	191	188	184	183	36	0

Figure 2. Kaplan–Meier Plot of the Probability of the Primary Composite Outcome.

The primary composite outcome was all-cause mortality, unplanned cardiac surgery, embolic events, or relapse of bacteremia with the primary pathogen, from randomization until 6 months after antibiotic treatment was completed. The oral treatment group shifted from intravenously administered antibiotics to orally administered antibiotics at a median of 17 days after the start of treatment. The inset shows the same data on an enlarged y axis.

Subgroup	Intravenous Treatment	Oral Treatment	Odds Ratio (95% CI)	P Value for Interaction
	no. of events/total no. (%)			
All patients	24/199 (12.1)	18/201 (9.0)	0.72 (0.37–1.36)	
Age				0.34
≤65.5 yr	9/83 (10.8)	7/91 (7.7)	0.68 (0.23–1.93)	
>65.5 yr	15/116 (12.9)	11/110 (10.0)	0.75 (0.32–1.70)	
Sex				0.19
Female	5/50 (10.0)	6/42 (14.3)	1.50 (0.42–5.59)	
Male	19/149 (12.8)	12/159 (7.5)	0.56 (0.26–1.18)	
Diabetes				0.51
Yes	8/36 (22.2)	4/32 (12.5)	0.50 (0.12–1.78)	
No	16/163 (9.8)	14/169 (8.3)	0.83 (0.39–1.76)	
Renal disease				0.40
Yes	5/25 (20.0)	5/21 (23.8)	1.25 (0.31–5.24)	
No	19/174 (10.9)	13/180 (7.2)	0.64 (0.30–1.32)	
Bacteria				0.94
Streptococci	10/104 (9.6)	8/92 (8.7)	0.90 (0.33–2.37)	
Enterococcus faecalis	7/46 (15.2)	4/51 (7.8)	0.47 (0.12–1.69)	
Staphylococcus aureus	3/40 (7.5)	3/47 (6.4)	0.84 (0.15–4.78)	
Coagulase-negative staphylococci	4/10 (40.0)	3/13 (23.1)	0.45 (0.07–2.72)	
Surgical treatment			0.47 (0.10–1.84)	0.50
Yes	6/75 (8.0)	3/77 (3.9)	0.81 (0.39–1.69)	
No	18/124 (14.5)	15/124 (12.1)		
Type of valve			0.48 (0.15–1.37)	0.35
Prosthetic heart valve	11/53 (20.8)	6/54 (11.1)	0.92 (0.40–2.09)	
Native heart valve	13/146 (8.9)	12/146 (8.2)		
Involved valve			0.65 (0.28–1.47)	0.56
Aortic valve	16/109 (14.7)	11/109 (10.1)	0.73 (0.20–2.56)	
Mitral valve	6/65 (9.2)	5/72 (6.9)		

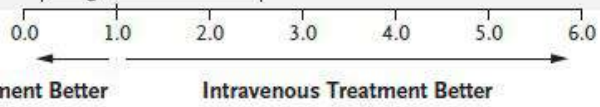


Figure 3. Rates of the Primary Outcome in Prespecified Subgroups.

tratamiento antibiótico oral
experiencia personal

tratamiento de metástasis sépticas: ocasionalmente

intención curativa: *Coxiella burnetii*

tratamiento antibiótico oral
experiencia GAMES

4318 episodios (2008 – 2017)

↓

464 casos (10,7%) recibieron tratamiento antibiótico oral

etiología	número (%)
Staphylococcus spp.	183 (39,4)
Streptococcus spp.	97 (20,9)
Enterococcus spp.	37 (8,0)
etiología no filiada	29 (6,3)
Candida spp.	24 (5,2)
Coxiella burnetii	24 (5,2)

119 casos (25,6%) – tratamiento presumiblemente supresor

evolución al año	número (%)
curación	305 (65,7)
mortalidad	18 (3,9)
recidiva	9 (1,9)

dalbavancina

Clinical Infectious Diseases

BRIEF REPORT

Dalbavancin as Primary and Sequential Treatment for Gram-Positive Infective Endocarditis: 2-Year Experience at the General Hospital of Vienna

Selma Tobudic,[1] Christina Forstner,[1,2] Heinz Burgmann,[1] Heimo Lagler,[1] Michael Ramharter,[1,3] Christoph Steininger,[1] Matthias (G) Vossen,[1] Stefan Winkler,[1] and Florian Thalhammer[1]

[1]Department of Medicine I, Division of Infectious Diseases and Tropical Medicine, Medical University of Vienna, Austria; and [2]Institute for Infectious Diseases and Infection Control, Jena University Hospital, and [3]Bernhard Nocht Hospital for Tropical Diseases, Bernhard Nocht Institute for Tropical Medicine and University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Clinical Infectious Diseases® 2018;67(5):795–8

estudio retrospectivo

2015 - 2016

31 pacientes (27 analizados)

administración semanal de 500 mg (dosis de carga 1000 mg), n = 9

administración bisemanal de 1000 mg (dosis de carga 1500 mg), n = 18

The clinical outcomes and safety of dalbavancin as primary and sequential treatment of gram-positive bacteremia with infective endocarditis were evaluated retrospectively. The clinical success rate was high (92.6%), but in 24 of 27 patients dalbavancin was used only after clearance of bacteria from the bloodstream.

Keywords. dalbavancin; endocarditis; Gram-positive infection.

Duration of Dalbavancin Therapy, wk	Patient No.	Types of IE	Pathogen	Therapy Before Dalbavancin (Duration, wk)	Reason for Change to Dalbavancin Therapy	Failure of Dalbavancin Treatment	Adverse Effects	Regimen (Once or Twice Weekly)
1 (n = 1)	1	Prosthetic valve	*Enterococcus faecalis*	Vancomycin (3)	Not documented	Death	No	Once
2 (n = 3)	2	Native valve	*Staphylococcus aureus*	Flucloxacillin and fosfomycin (2) cefazoline and daptomycin (4)	Poor venous access	No	No	Once
	3	Native valve	*S. aureus*	Flucloxacillin and daptomycin (5)	OPAT	No	No	Twice
	4	Native valve	*S. aureus*	Cefuroxime and daptomycin (4)	Poor venous access	No	No	Twice
4 (n = 5)	5	Native valve	*E. faecalis*	Ceftriaxone and ampicillin (2)	OPAT	No	No	Once
	6	Prosthetic valve	*Streptococcus equi*	Penicillin G (1)	OPAT	No	Nausea	Twice
	7	CDE	*Staphylococcus epidermidis*	Cefazoline and fosfomycin (4)	OPAT	No	No	Twice
	8	CDE	*S. epidermidis*	Daptomycin (4)	OPAT	No	No	Twice
	9	Native valve	*Streptococcus mitis*	Ceftriaxone and gentamycin (2)	OPAT	No	No	Twice
6 (n = 10)	10	Prosthetic valve	*S. aureus*	Flucloxacillin and rifampicin (2)	OPAT[a]	No	No	Once
	11	Native valve	*Staphylococcus hominis*	Flucloxacillin and daptomycin (2)	OPAT	No	No	Once
	12	CDE	*Streptococcus* spp., *S. epidermidis*	Daptomycin (5 d), vancomycin (2)	OPAT	No	No	Once
	13	Prosthetic valve	*Streptococcus equinus*	Penicillin G (1)	OPAT	No	No	Twice
	14	Suspected prosthetic valve	*Streptococcus sanguinis*	No	OPAT	No	RCI	Twice
	15	Native valve	*E. faecalis*	Ceftriaxone and ampicillin (1)	OPAT	No	No	Twice
	16	Native valve	*Aerococcus urinae*	Penicillin G (2)	OPAT	No	No	Twice
	17	Native valve	*S. aureus*	Flucloxacillin and daptomycin (1)	Poor venous access	No	No	Twice
	18	Native valve	*S. aureus*	Flucloxacillin and fosfomycin (1)	OPAT	No	No	Twice
	19	Native valve	*S. sanguinis, S. hominis*	Flucloxacillin and ampicillin (1)	OPAT	No	No	Twice
>6 (n = 8)	20	Native valve	*E. faecalis*	No	OPAT	No	No	Once
	21	Native valve	*S. sanguinis*	Vancomycin (1), daptomycin (1)	OPAT	No	No	Once
	22	CDE	*S. epidermidis*	No	OPAT	No	No	Once
	23	CDE	*S. aureus*	Flucloxacillin (1)	OPAT	Resistance	No	Once
	24	Native valve	*S. aureus*	Ceftriaxone (1), daptomycin (1)	OPAT	No	No	Twice
	25	Prosthetic valve	*S. aureus*	Flucloxacillin and rifampicin (1)	OPAT	No	No	Twice
	26	Prosthetic valve	*S. sanguinis*	Penicillin G (1)	OPAT	No	No	Twice
	27	Native valve IE	*Staphylococcus caprae*	Cefazoline (1)	OPAT	No	No	Twice

DALBAVANCINA COMO TRATAMIENTO DE SECUENCIACIÓN EN PACIENTES CON ENDOCARDITIS Y/O BACTERIEMIA POR COCOS GRAM POSITIVOS.

C. Hidalgo-Tenorio(1), S. De Jesús(1), D. Vinuesa (2), A. Plata (3), P. Martín Dávila(4), Simona Iftimie (5), Belén Loeches (6) L. E. López Cortés (7), M.C. Fariñas (8), R. Javier Martinez (1), P. Muñoz (9), M. Arenas-Miras (10), Fco. Martinez (11), JM Miró (12), C. Herrero (13), Elena Bereciartua (14)y J. Pasquau Liaño(1).

Tabla 1. Características basales de los pacientes.

	N = 80
Edad, mediana (IQR)	69 (54-78)
Hombres, n (%)	58 (72,5)
Índice Charlson, n (%)	2 (1-4)
Tipo de infección, n (%)	
- El definida	32 (40)
- El probable	3 (3,8)
- Bacteriemia complicada	30 (37,5)
- Bacteriemia no complicada	15 (18,8)
Válvula, n (%)	
- Aórtica	18 (66.7)
- Mitral	8 (29,6)
- Tricúspide	1 (3,7)
Endocarditis, n (%)	N=35
- Nativa	12 (33,3)
- Protésica precoz	5 (13,9)
- Protésica tardía	11 (30,9)
- Sobre marcapasos	8 (22,2)

Tabla 2. Microorganismos implicados.

Agente etiológico, n (%)	N=80
- SAMS	19 (23,8)
- SAMR	12 (15)
- SCN	31 (38,8)
- Streptococo	6 (7,5)
- *E. faecalis*	4 (5)
- *E. faecium*	2 (2,5)
- *Abiotrophia defectiva*	1 (1,3)

Tabla 3. Antibióticos previos y motivo de administración de DBV.

	N=80
Días tratamiento previo, mediana (IQR)	18,5 (11-32)
Tratamiento antibiótico previo, n (%)	76 (95)
- Dapto previo	46 (58,2)
- Ceftriaxona previo	19 (24,1)
- Linezolid previo	12 (15,2)
- Vancomicina previa	18 (22,8)
Motivo administración de la DBV, n (%)	
- Facilitar el alta	65 (85,5)
- Fracaso tratamiento previo	4 (5,3)
- Toxicidad	2 (2,6)

- **De los 80 pacientes, 64 tienen ya 90 días de seguimiento:**
  - Presentaron resolución clínica de la infección (100%), y microbiológica 98% (HC negativos, pero 1 cultivo de válvula positivo).
  - Los casos de EI que requirieron CIRUGÍA recibieron la Dalbavancina tras esta, menos 2 (uno se le administró el mismo día de la explantación; y el otro tenía EI protésica por SCN que se trató 6 semanas con ab (con 1500mg de DBV) ingresó para recambio valvular programado y en la válvula que se envio a cultivar se aisló SCN y *P. acnes* en muy escasa cantidad.
  - Un paciente falleció (HD con sepsis con bacteriemia por BGN) y dos reingresaron, por motivos distintos a la bacteriemia por CGP, y tras la resolución de la infección.
  - Tres pacientes experimentaron efectos adversos (un paciente con astenia, otro fiebre con tiritona autolimitadas y otro empeoramiento de la función renal).
- **El tratamiento con DBV permitió una anticipación del alta en 67 pacientes (85,9%), con un ahorro total de 1144 días [media de 15,2 días/paciente, (rango 0-72)].**

dalbavancina
experiencia (¿actualizada?) GAMES

4318 episodios (2008 – 2017) pertenecientes a 35 hospitales

11 casos de 3 hospitales (9, 1, 1)

S. aureus 4, *S. gallolyticus* 3, *S. epidermidis* 2, *S. viridans* 1, *E. faecalis* 1

tratamientos domiciliarios, al alta

vivos

11 centros respondieron a la encuesta

30-35 casos

predominio de *S. aureus*, también *S. viridans*, *S. gallolyticus* y enterococo

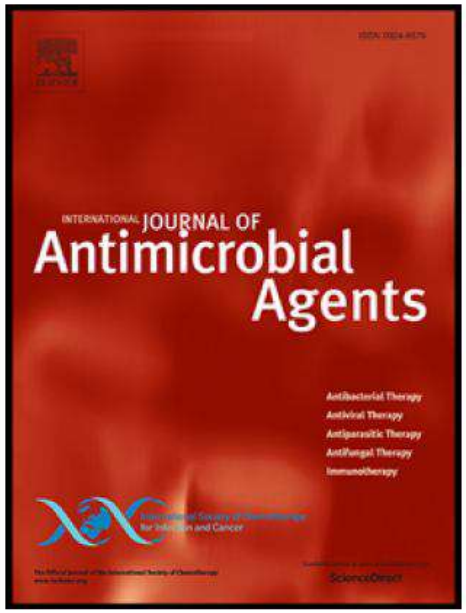
tratamiento de continuación

dificultad con anticoagulantes 1

éxitus 1

teicoplanina

Accepted Manuscript



Teicoplanin for treating enterococcal infective endocarditis: a retrospective observational study from a referral center

Laura Escolà-Vergé , Nuria Fernández-Hidalgo ,
Dolors Rodríguez-Pardo , Carlos Pigrau ,
Juan José González-López , Rosa Bartolomé , Benito Almirante

PII: S0924-8579(18)30295-4
DOI: https://doi.org/10.1016/j.ijantimicag.2018.10.003
Reference: ANTAGE 5560

Table 1. Demographic features, comorbidities, etiology, presumed source of infection, and echocardiography findings in 22 episodes of enterococcal infective endocarditis treated with teicoplanin.

	Overall (N=22)	Teicoplanin 1st line therapy (N=9)	Teicoplanin salvage therapy (N=13)
Demographics			
Age, years, median (IQR)	71.5 (58.3-78)	75 (64.5-83)	64 (53.5-74.5)
Male sex	17 (77.3%)	7 (77.8%)	10 (76.9%)
Comorbidities			
Charlson comorbidity index, median (IQR)	4.5 (3-7)	6 (4.5-8.5)	3 (2-6)
Chronic renal failure[a]	9 (40.9%)	5 (55.6%)	4 (30.8%)
Diabetes mellitus	7 (31.8%)	3 (33.3%)	4 (30.8%)
Transplantation	3 (13%)	2 (22.2%)	1 (7.1%)
Neoplasm	3 (13%)	2 (22.2%)	1 (7.1%)
Liver cirrhosis	1 (4.3%)	1 (11.1%)	0
HIV infection	1 (4.3%)	1 (11.1%)	0
Etiology			
Enterococcus faecalis	14 (63.6%)	1 (11.1%)	13 (100%)
Enterococcus faecium	8 (36.4%)	8 (88.9%)	0

mediana de duración del tratamiento antibiótico en supervivientes

total 53 días (RIC 42,5 – 61)

teicoplanina 27 días (17 – 41,5)

dosis 10 mg/kg/día (10 – 10,8), en monoterapia

razones para administrar la teicoplanina

resistencia a β-lactámicos 40,9%

efectos adversos del tratamiento antibiótico previo 31,8%

tratamiento ambulatorio 27,3%

evolución

efectos adversos en 2 casos: leucopenia 1, fiebre y rash 1

muerte durante el tratamiento en 5 pacientes (22,7%): primera línea 4, rescate 1

muerte durante el seguimiento 2

no recidivas (mediana de seguimiento 43,2 meses [22,1 – 69,1])

mensajes

teicoplanina se puede utilizar como primera línea de tratamiento en endocarditis por *E. faecium*

teicoplanina se puede utilizar como rescate / secuenciación en endocarditis por *E. faecalis* en caso de aparición de efectos adversos con tratamientos antibióticos previos o para facilitar el alta domicilio

ampicilina

● AMPICILINA

Aminopenicilina $C_{16}H_{19}N_3O_4S$ **PM** 349,4

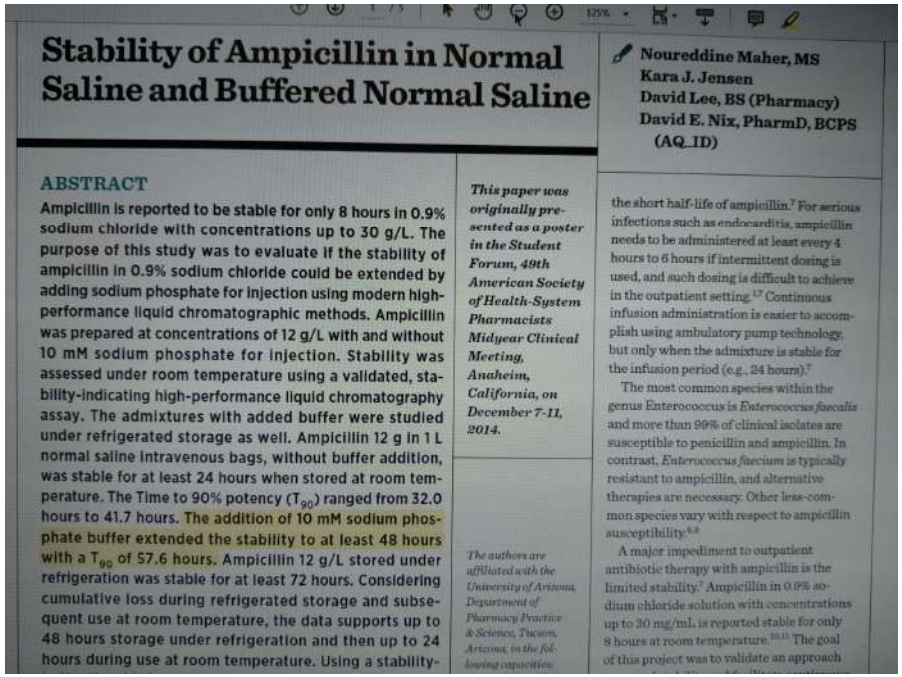
MECANISMO DE ACCIÓN Y ESPECTRO. Véase penicilinas, pág. 16. Microorganismos sensibles. Cocos grampositivos: neumococo, estreptococos, *Enterococcus faecalis, Staphylococcus saprophyticus* y *Peptostreptococcus*. Bacilos grampositivos: *Clostridium, Corynebacterium diphtheriae, Bacillus anthracis, Listeria, Erysipelothrix* y *Actinomyces*. Cocos gramnegativos: *Neisseria meningitidis*. Bacilos gramnegativos: *Escherichia coli, Proteus mirabilis, Salmonella* spp, *Shigella* spp, *Haemophilus influenzae, Eikenella corrodens, Bordetella pertussis, Pasteurella multocida, Prevotella* spp y *Fusobacterium* spp (tasas de resistencia por producción de betalactamasas, variables según el área geográfica). Otros microorganismos sensibles: *Leptospira*. Ampicilina es algo más activa que amoxicilina frente a *Shigella* y *Haemophilus*. Microorganismos resistentes: *Staphylococcus aureus, E. faecium*, el resto de enterobacterias no mencionadas en el apartado anterior, bacilos gramnegativos no fermentadores y la mayoría de cepas de *N. gonorrhoeae, M. catarrhalis*. **Punto de corte:** enterobacterias CIM ≤8 mg/L, *Staphylococcus* spp[1] y *Enterococcus* spp CIM ≤4 mg/L. Estreptococos beta-hemolíticos[1], *S. pneumoniae* y estreptococos del grupo «viridans» CIM ≤0,5 mg/L. *H. influenzae* y *M. catarrhalis* CIM ≤1 mg/L. *N. meningitidis* CIM ≤0,12 mg/L. Microorganismos anaerobios, grampositivos CIM ≤4 mg/L, gramnegativos CIM ≤0,5 mg/L

DOSIS. Adulto: oral 0,5-1 g/4-8 h (biodisponibilidad del 40 %; la administración con comida disminuye la absorción –administrar en ayunas–). Por vía iv 100-300 mg/kg (peso ajustado)/día (1-2 g/4-6 h)[2]. **Niño:** oral 50 mg/kg/día en 4 dosis. Por vía im o iv 100-200 mg/kg/día en 4 dosis[3]

- **Insuficiencia renal:** FG >50: sin cambios. FG 30-50: iv 1-2 g/6 h. FG 10-30: iv 1-2 g/8 h. FG <10: iv 1 g/12 h. Hemodiálisis: dializa 20-50 %. Diálisis peritoneal: dializa <5 %. **Insuficiencia hepática:** sin cambios
- **Embarazo:** (B) probablemente seguro. **Lactancia:** puede emplearse

Comentarios. [1]Se consideran sensibles si lo son a penicilina. [2]Estabilidad de la dilución para la administración por vía iv: 8 h a 25 °C. [3]En meningitis dosis de 200-400 mg/kg/día iv en 4 dosis

una conversación con Juan Gálvez...



Stability of Ampicillin in Normal Saline and Buffered Normal Saline

Noureddine Maher, MS
Kara J. Jensen
David Lee, BS (Pharmacy)
David E. Nix, PharmD, BCPS (AQ_ID)

ABSTRACT

Ampicillin is reported to be stable for only 8 hours in 0.9% sodium chloride with concentrations up to 30 g/L. The purpose of this study was to evaluate if the stability of ampicillin in 0.9% sodium chloride could be extended by adding sodium phosphate for injection using modern high-performance liquid chromatographic methods. Ampicillin was prepared at concentrations of 12 g/L with and without 10 mM sodium phosphate for injection. Stability was assessed under room temperature using a validated, stability-indicating high-performance liquid chromatography assay. The admixtures with added buffer were studied under refrigerated storage as well. Ampicillin 12 g in 1 L normal saline intravenous bags, without buffer addition, was stable for at least 24 hours when stored at room temperature. The Time to 90% potency (T_{90}) ranged from 32.0 hours to 41.7 hours. The addition of 10 mM sodium phosphate buffer extended the stability to at least 48 hours with a T_{90} of 57.6 hours. Ampicillin 12 g/L stored under refrigeration was stable for at least 72 hours. Considering cumulative loss during refrigerated storage and subsequent use at room temperature, the data supports up to 48 hours storage under refrigeration and then up to 24 hours during use at room temperature. Using a stability-

This paper was originally presented as a poster in the Student Forum, 49th American Society of Health-System Pharmacists Midyear Clinical Meeting, Anaheim, California, on December 7-11, 2014.

The authors are affiliated with the University of Arizona, Department of Pharmacy Practice & Science, Tucson, Arizona, in the following capacities:

the short half-life of ampicillin.[7] For serious infections such as endocarditis, ampicillin needs to be administered at least every 4 hours to 6 hours if intermittent dosing is used, and such dosing is difficult to achieve in the outpatient setting.[1,7] Continuous infusion administration is easier to accomplish using ambulatory pump technology, but only when the admixture is stable for the infusion period (e.g., 24 hours).[7]

The most common species within the genus Enterococcus is *Enterococcus faecalis* and more than 90% of clinical isolates are susceptible to penicillin and ampicillin. In contrast, *Enterococcus faecium* is typically resistant to ampicillin, and alternative therapies are necessary. Other less-common species vary with respect to ampicillin susceptibility.[8,9]

A major impediment to outpatient antibiotic therapy with ampicillin is the limited stability.[7] Ampicillin in 0.9% sodium chloride solution with concentrations up to 30 mg/mL is reported stable for only 8 hours at room temperature.[10,11] The goal of this project was to validate an approach

ampicilina 24 g/L suero fisiológico (con y sin 10 mEq de fosfato potásico)

T0, T6 y T24 a temperatura ambiente (30ºC)

solución original: pH 8,6 – 8,2

solución tamponada: pH 7,5 – 7,5

Journal of Pharmacy Practice
1-3
© The Author(s) 2018
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/0897190018804964
journals.sagepub.com/home/jpp
SAGE

Continuous Infusion Ampicillin for the Outpatient Management of Enterococcal Endocarditis: A Case Report and Literature Review

Paul O. Lewis, PharmD, BCPS (AQ-ID)[1], Abigail Jones, PharmD, BCPS[1], Rachel J. Amodei, PharmD[2], and Dima Youssef, MD[3]

ceftarolina

no news bad news

J Antimicrob Chemother 2014
doi:10.1093/jac/dku085
Advance Access publication 28 March 2014

Salvage treatment of methicillin-resistant staphylococcal endocarditis with ceftaroline: a multicentre observational study

Pierre Tattevin[1,2]*, David Boutoille[2,3], Virginie Vitrat[4], Nicolas Van Grunderbeeck[5], Matthieu Revest[1,2], Mathieu Dupont[6], Serge Alfandari[7] and Jean-Paul Stahl[8]

desde entonces...

5 casos clínicos (combinación con daptomicina y cotrimoxazol)

1 artículo de revisión (!!!!)

ceftarolina
IDWeek 2018

póster #2426

Table 3: Summary of Ceftaroline-Associated Neutropenia in Studies with Control Group

Study	Ceftaroline Use	Risk Factors	Incidence of Neutropenia
Furtek KJ et al.[1]	≥7 days	Duration of ceftaroline	7% (5/67)
LaVie KW et al.[4]	≥7 days	Female sex & low BMI	18% (7/39)
Turner RB et al.[8]	≥14 days	None identified	17% (9/53)
Current Study	≥7 days	None identified	7% (4/56)
All Studies	**≥7-14 days**	------	**12% (25/215)**

Table 1: Details of Current Cases of Ceftaroline-Associated Neutropenia

Age/ Sex	Indication	Dose	Duration (days)	Nadir ANC (cells/mm^3)	Days of Neutropenia
66 M	Prosthetic knee infection	300 mg IV q8 hr	8	1205	2
59 F	Bacteremia, endocarditis, diskitis/osteomyelitis	400 mg IV q8 hr	20	20	10
26 F	Bacteremia, endocarditis	600 mg/400 mg IV q8 hr	21	5	7
44 M	Osteomyelitis, endocarditis	600 mg IV q12 hr	23	1472	2

ceftarolina
experiencia GAMES

4318 episodios (2008 – 2017) pertenecientes a 35 hospitales

8 casos de 3 hospitales (4, 3, 1)

S. epidermidis 3, *S. aureus* 2, *E. faecalis 1, S. gallolyticus* 1, *S. salivarius* 1

tratamiento de rescate 7, primera intención 1

éxitus 2 (*S. epidermidis*)

11 centros respondieron a la encuesta

15-20 casos

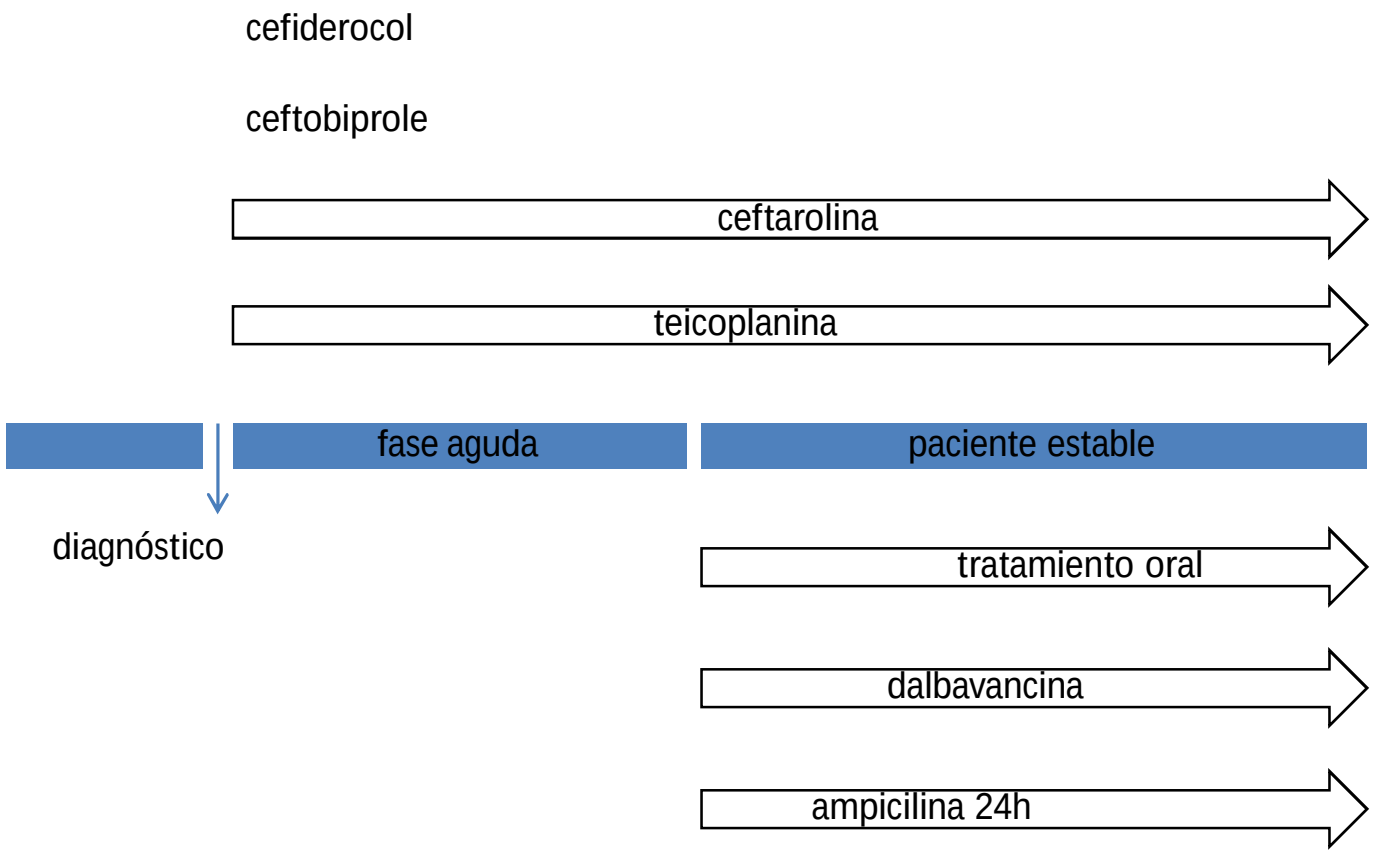
Staphylococcus spp. 95% (predominio de *S. aureus*)

primera opción terapéutica en un número reducido de casos, mayoría rescate

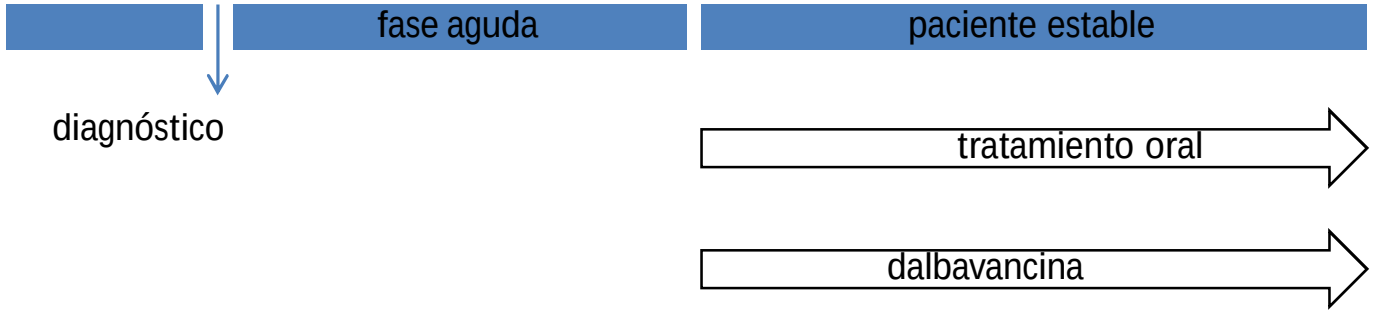
sin efectos secundarios

curación en todos los casos

resumen


cefiderocol
ceftobiprole
ceftarolina
teicoplanina
fase aguda
paciente estable
diagnóstico
tratamiento oral
dalbavancina
ampicilina 24h

el factor económico



dalbavancina 1,5 g i.v. = 1.342 €

(2 semanas)

Penicillin and methicillin sensitive *Staphylococcus aureus* and coagulase-negative staphylococci:

1) Amoxicillin 1 g x 4 and [redacted]
2) Amoxicillin 1 g x 4 and rifampicin 0.6 g x 2 — 13,3 € / semana
3) Linezolid 0.6 g x 2 and [redacted]
4) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2 — 46,2 € / semana

Methicillin sensitive *Staphylococcus aureus* and coagulase-negative staphylococci

1) Dicloxacillin 1 g x 4 and [redacted]
2) Dicloxacillin 1 g x 4 and rifampicin 0.6 g x 2 — 21 € / semana
3) Linezolid 0.6 g x 2 and [redacted]
4) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2 — 46,2 € / semana

Methicillin resistant coagulase-negative staphylococci

1) Linezolid 0.6 g x 2 and [redacted]
2) Linezolid 0.6 g x 2 and rifampicin 0.6 g x2 — 46,2 € / semana

Enterococcus faecalis:

1) Amoxicillin 1 g x 4 and rifampicin 0.6 g x 2 — 13,3 € / semana
2) Amoxicillin 1 g x 4 and moxifloxacin 0.4 g x 1 — 32,06 € / semana
3) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2 — 46,26 € / semana
4) Linezolid 0.6 g x 2 and moxifloxacin 0.4 g x 1 — 64,96 € / semana

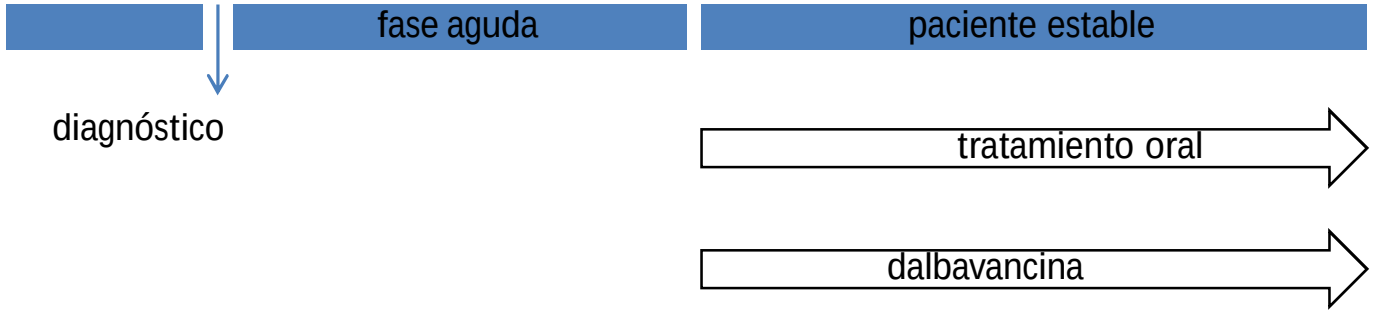
Streptococci with a minimal inhibitory concentration for penicillin of <1 mg/L:

1) Amoxicillin 1 g x 4 and rifampicin 0.6 g x 2 — 13,3 € / semana
2) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2 — 46,26 € / semana
3) Linezolid 0.6 g x 2 and moxifloxacin 0.4 g x1 — 64,96 € / semana

Streptococci with a minimal inhibitory concentration for penicillin of ≥1 mg/L:

1) Linezolid 0,6 g x2 and rifampicin 0.6 g x 2 — 46,26 € / semana
2) Moxifloxacin 0.4 g x 1 and rifampicin 0.6 g x 2 — 38,36 € / semana
3) Moxifloxacin 0.4 g x 1 and clindamycin 06 g x3 — 42,84 € / semana

otros factores



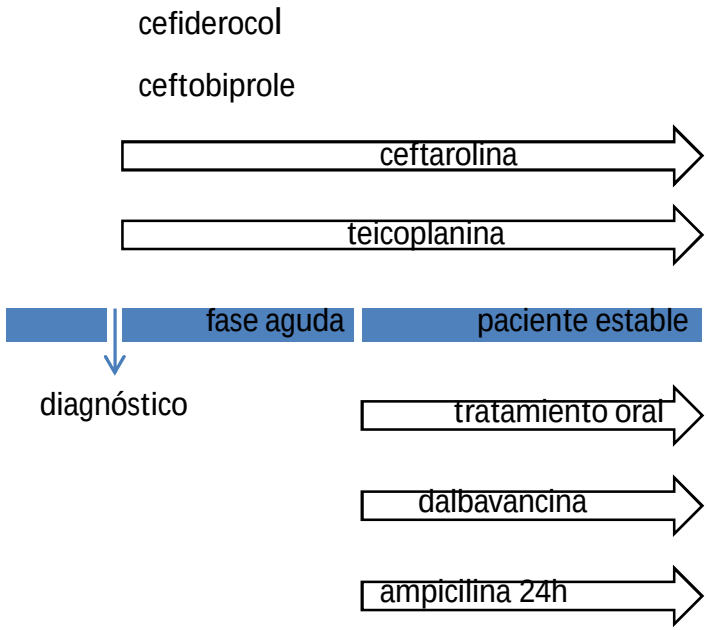
confianza

niveles plasmáticos

toxicidad

interacciones

conclusiones



selección adecuada de pacientes

importancia de la experiencia propia/ajena

equilibro efectividad / seguridad

factor económico

nufernan@gmail.com