Sociedad Española de Farmacia Hospitalaria

Jornada Grupo AFINF:

Actualización en Atención Farmacéutica en Enfermedades Infecciosas

AFinf

Nuevas vias de administración
Antibióticos Nebulizados

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Hospital de Mataró

Madrid
22 junio de 2016

Introducción

La neumonía es una de las infecciones mas frecuentes en el paciente crítico con una mortalidad entre 3 y 17 %

9 - 27% pacientes intubados desenvoluparan una NAVM, con una mortalidad asociada entre el 20 y 80%

Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia
American Thoracic Society/Infectious Diseases Society of America (ATS/ IDSA)
Eur Respir J 2006;27:158-64

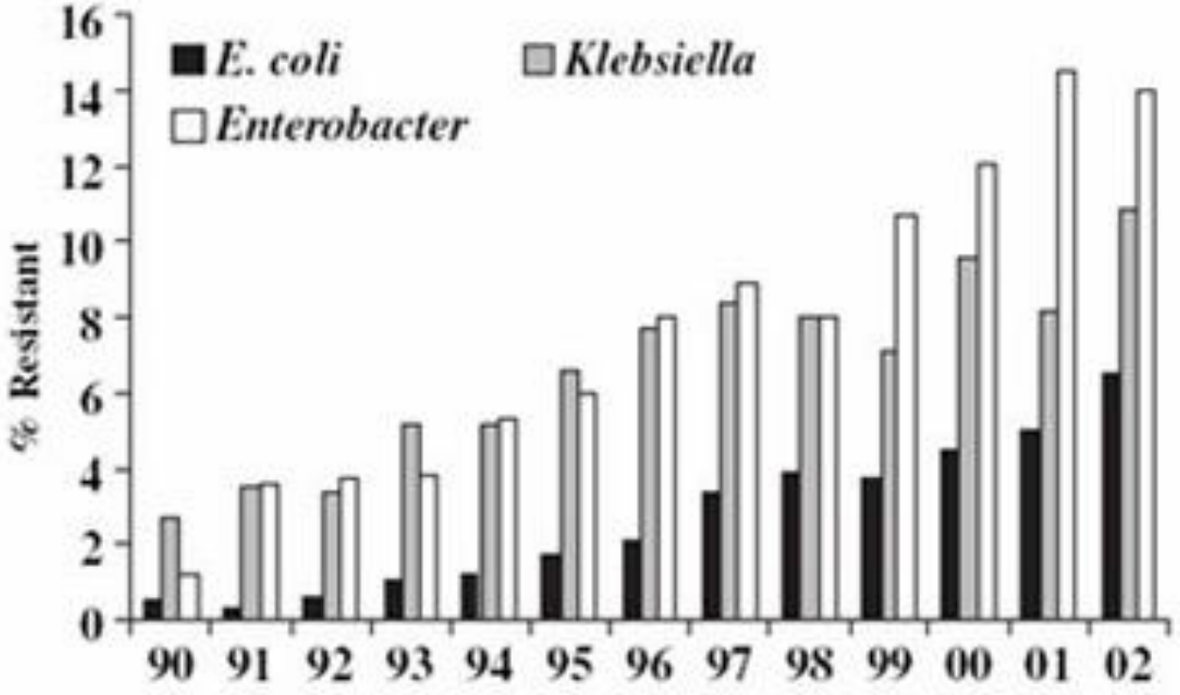
Epidemiological trends in invasive mechanical ventilation in the United States: A population-based study
Metha AB, Syeda SN, Wiener RS, et al
J Crit Care. 2015;30:1217–1221

Ventilator-associated pneumonia in the ICU
Kalanuria AA, Zai W, Mirski M
Crit Care. 2014;18:208

Estimating the attributable mortality of ventilator-associated pneumonia from randomized prevention studies
Melsen WG, Rovers M, Koeman M, et al
Crit Care Med. 2011;39:2736–2742

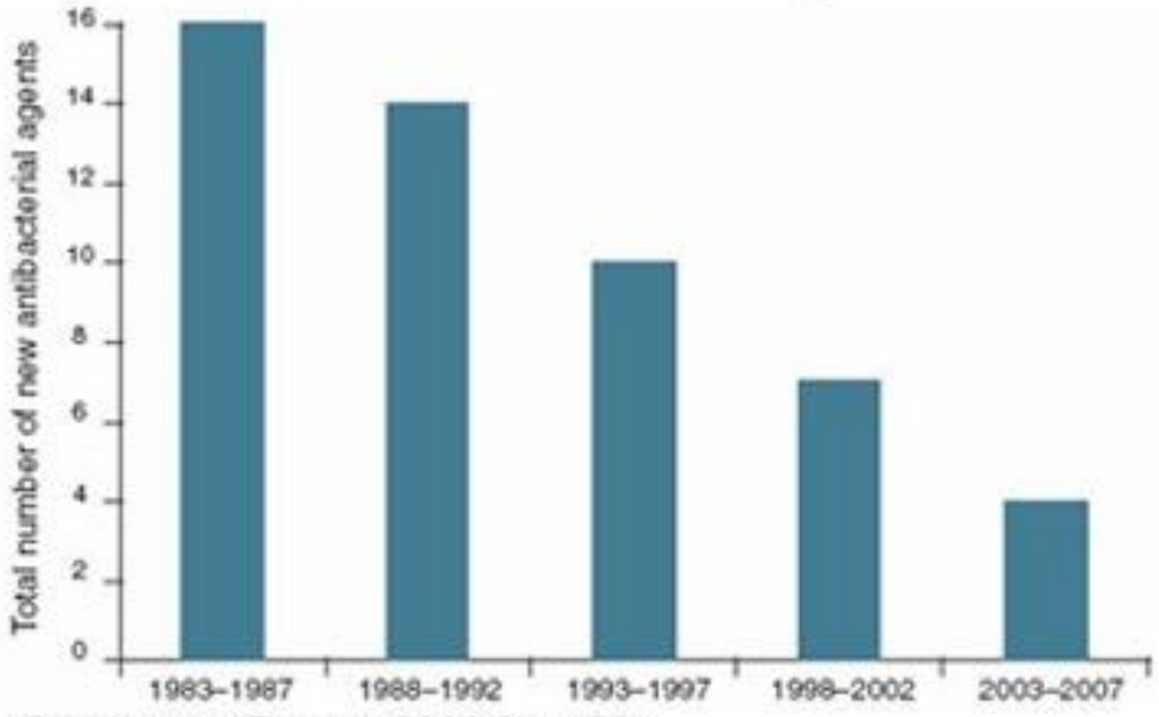
Cada día menos opciones terapéuticas…

A. Increase in drug resistance among pathogens



Source: Clinical Microbiol infect 2004; 10 (Suppl. 4): 1–9

B. Decreased number of new drugs in the market



Source: Nat Biotech 2006 24: 1521

Hace difícil utilizar el ATB adecuado en NAVM

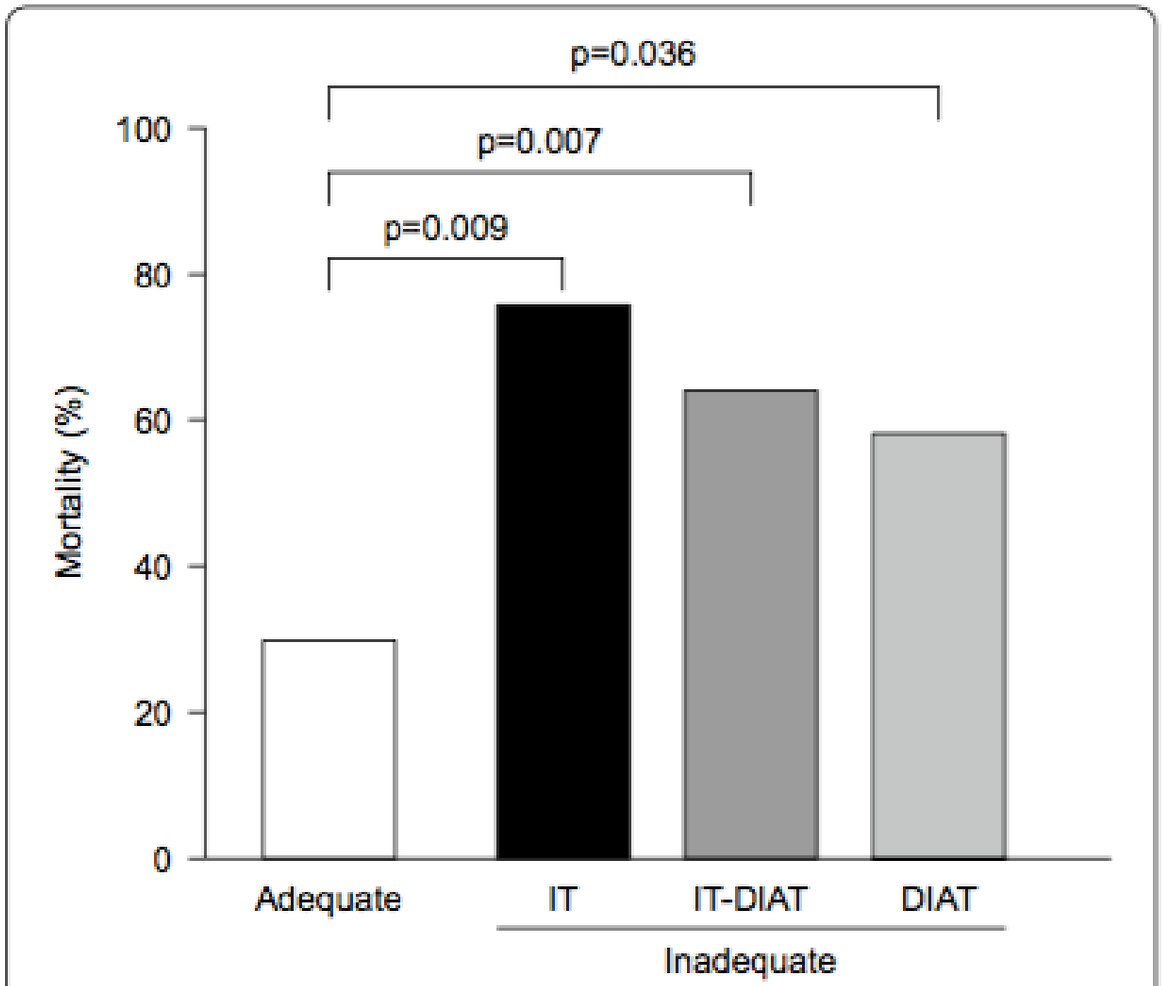


Fig. 1 Mortality rates observed in patients with ventilator-associated pneumonia who received adequate, inadequate (IT-DIAT inadequate), inappropriate therapy (IT) or delayed initiation of appropriate therapy (DIAT). Adapted from Ref. [5]. Figure reproduced with permission from the European Respiratory Society who are the copyright holders for this material

Appropiatness and delay to initiate therapy in ventilator-associated pneumonia

Luna C, Aruj P, Niederman M, Garzón J, Violi D, Prignoni A, Rios F, Baquero S, Gando S

Eur Respir J 2006;27:158-64

Buscando alternativas…

Vincent *et al. Critical Care* (2016) 20:133

Advances in antibiotic therapy in the critically ill

Jean-Louis Vincent[1*], Matteo Bassetti[2], Bruno François[3], George Karam[4], Jean Chastre[5], Antoni Torres[6], Jason A. Roberts[7], Fabio S. Taccone[1], Jordi Rello[8], Thierry Calandra[9], Daniel De Backer[10], Tobias Welte[11] and Massimo Antonelli[12]

A place for nebulized antibiotics in VAP?

Expert Rev Respir Med 2016 Jun 3:1-12

Can we improve clinical outcomes in patients with pneumonia treated with antibiotics in the intensive care unit?

David P. Nicolau,[1*] George Dimopoulos,[2] Tobias Welte[3] and Charles-Edouard Luyt[4,5]

Administration of antibiotics via aerosolization offers the opportunity to achieve very high antibiotic concentration to MIC ratios by delivering drug directly to the pulmonary tissues, potentially improving efficacy and reducing

Objetivos nebulización

Penetración pulmonar factor limitante

Aumentar dosis provocará efectos tóxicos

Deposición directa en pulmón y pobre absorción sistémica

Antibiotic penetration into lugn tissues
Hnoeybourne D et al
Thorax 1994;49:104-6

Penetration of vancomycin into human lung tissues
Cruciana M, Gatti G, Lazzarini L, Furlan G, Broccali G, Malena M, Franchini C, Concia E
J Antimicrob Chemother 1996;38:865-9

Steady-state pharmacokinetics and BAL concentration of colistin in critically ill patients after IV colistin methanesulfonate administration
Imberti R, Cusato M, Villani P, Carnevale L, Iotti G, Langer M, Regazzi M
Chest 2010;138:1333-0

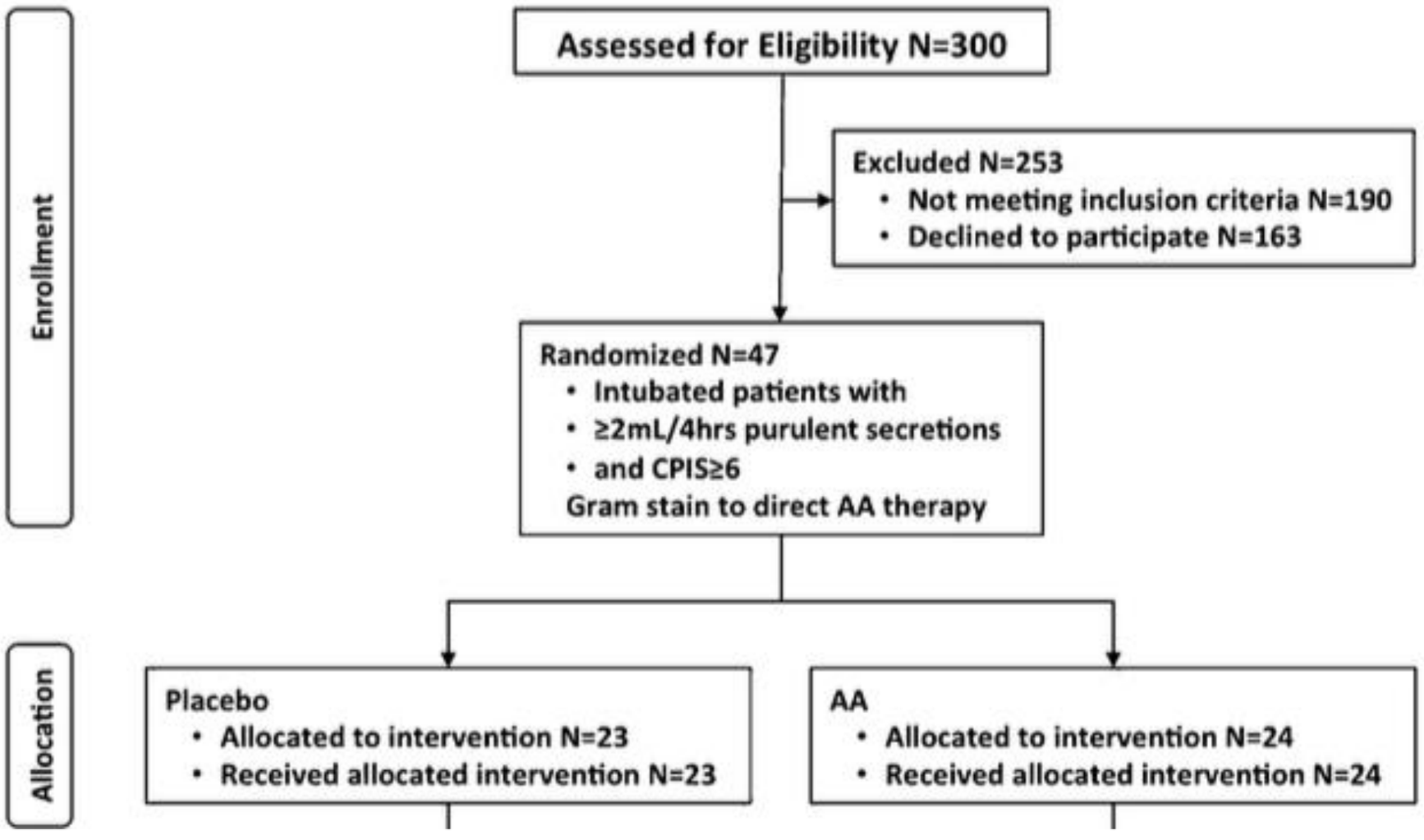
Absolute bioavailability and absoprtion characteristics of aerosolized tobramycin in adults with cystic fibrosis
Cooney G, Lum B, Tomaselli M, Fiel S
Clin Pharmacol 1994;34:255-9

Terapia nebulizada NO augmenta resistencias

Reduction of Bacterial Resistance with Inhaled Antibiotics in the Intensive Care Unit

Lucy B. Palmer and Gerald C. Smaldone

American Journal of Respiratory and Critical Care Medicine Volume 189 Number 10 | May 15 2014



AA (n = 16)

Placebo (n = 11

P value*

Definition of abbr
vancomycin-resis
Data from patien
*Fisher exact test

Organism

bacter sp.

bacter sp.

lla pneumoniae, MRSA

bacter sp.

nonas aeruginosa; VRE =

Terapia nebulizada reduce uso parenteral

NKTR-061 (Inhaled Amikacin) Reduces Intravenous Antibiotic Use in Intubated Mechanically Ventilated Patients During Treatment of Gram-Negative Pneumonia

M.S. Niederman[1], J. Chastre[2], K. Corkery[3], A. Marcantonio[3], J.B. Fink[3], C.E. Luyt[2], M. Sanchez[4] and The Amikacin Study Group[5]

[1]Winthrop University Hospital, Mineola, New York, USA; [2]Hôpital Pitié-Salpétrière, Paris, France; [3]Nektar Therapeutics, San Carlos, CA, USA; [4]Hospital Universitario Principe de Asturias, Madrid, Spain

Critical Care Volume 11 Suppl 2, 2007

27th International Symposium on Intensive Care and Emergency Medicine

Brussels, Belgium, 27–30 March 2007

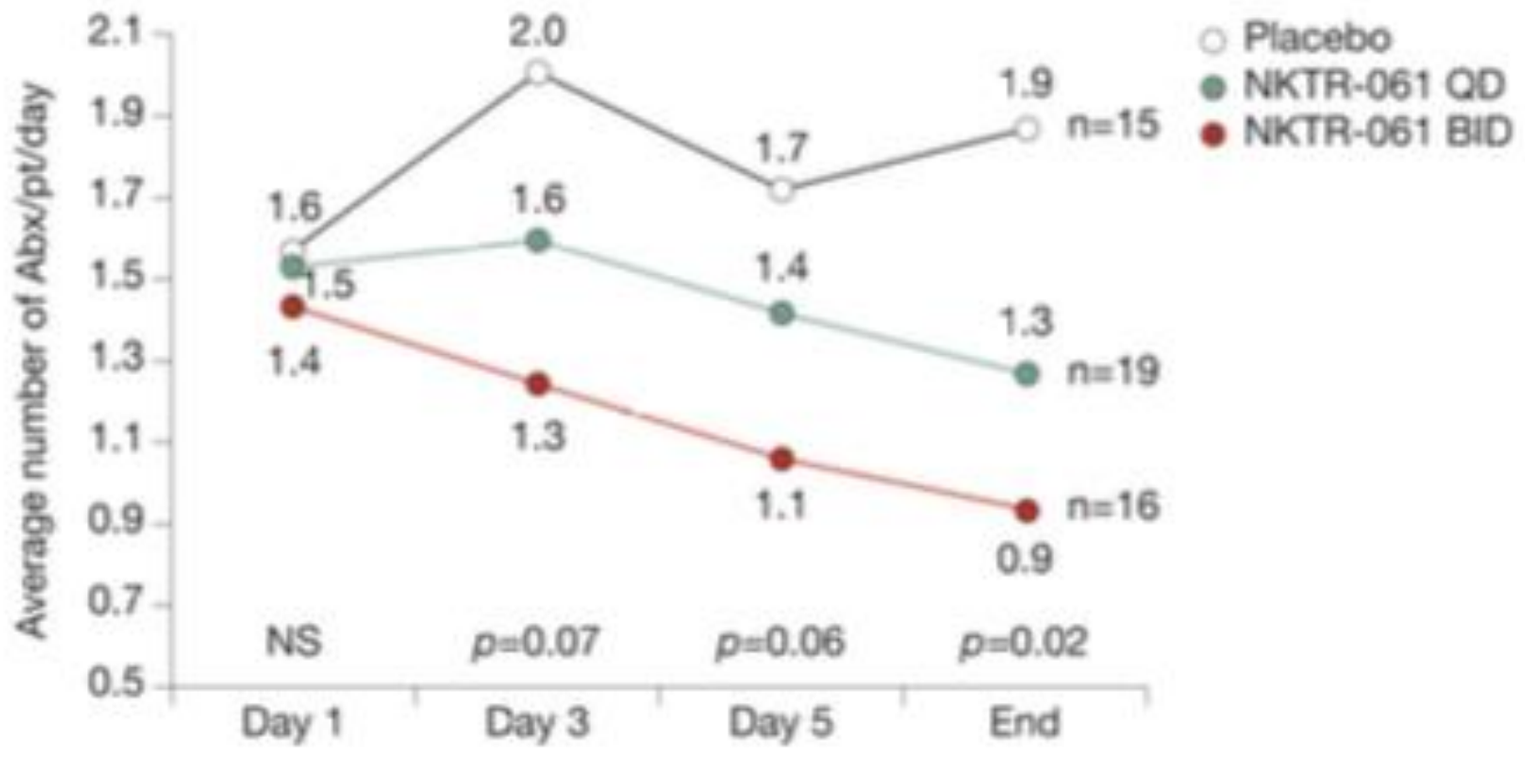
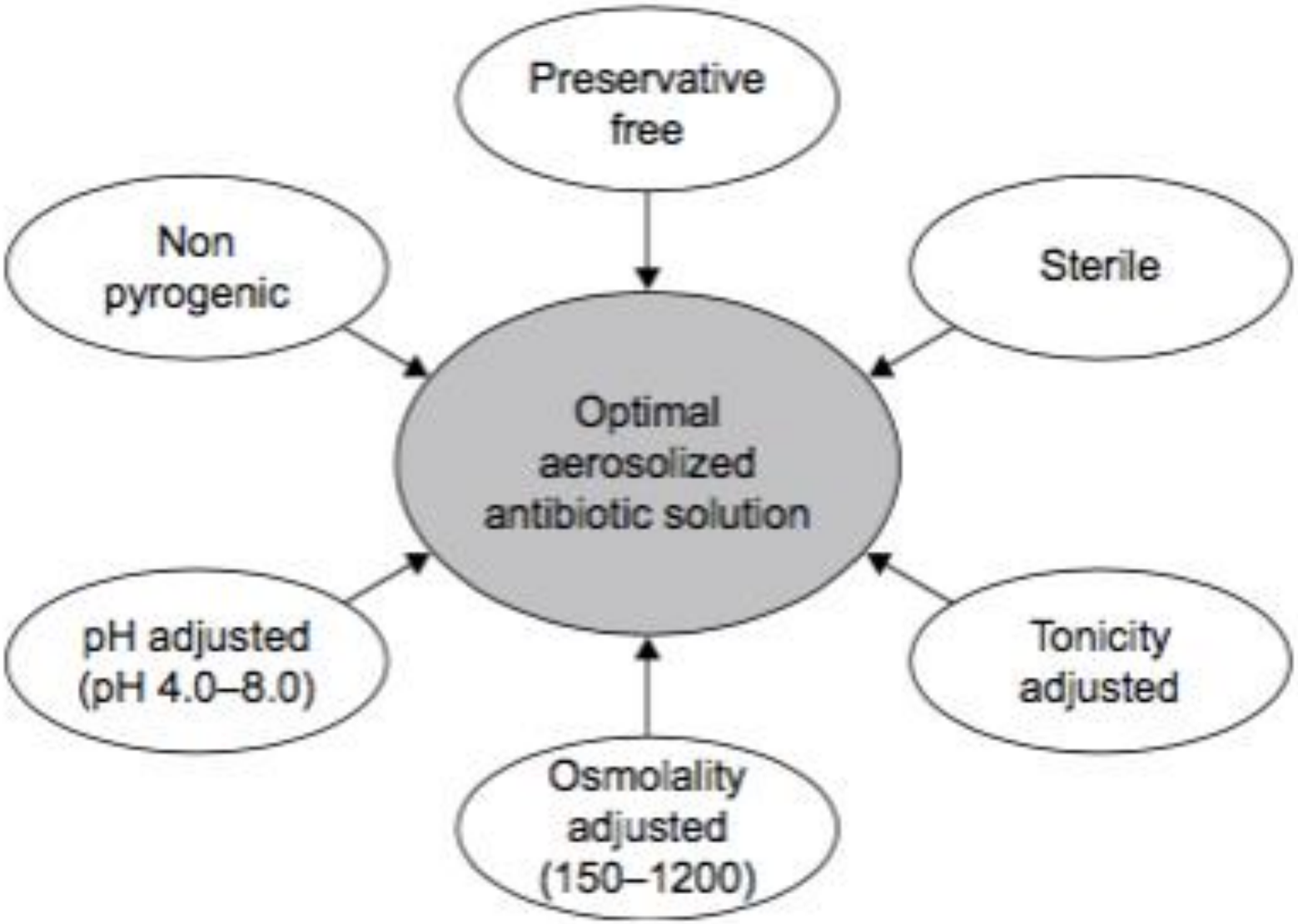


Figure 3. Number of systemic antibiotics administered each day with placebo, QD and BID dosing of NKTR-061. There was a significant decline in IV antibiotic utilization with the BID dose (p=0.02) over time with NKTR-061.

Characteristics of an ideal nebulized antibiotic for the treatment of pneumonia in the intubated patient

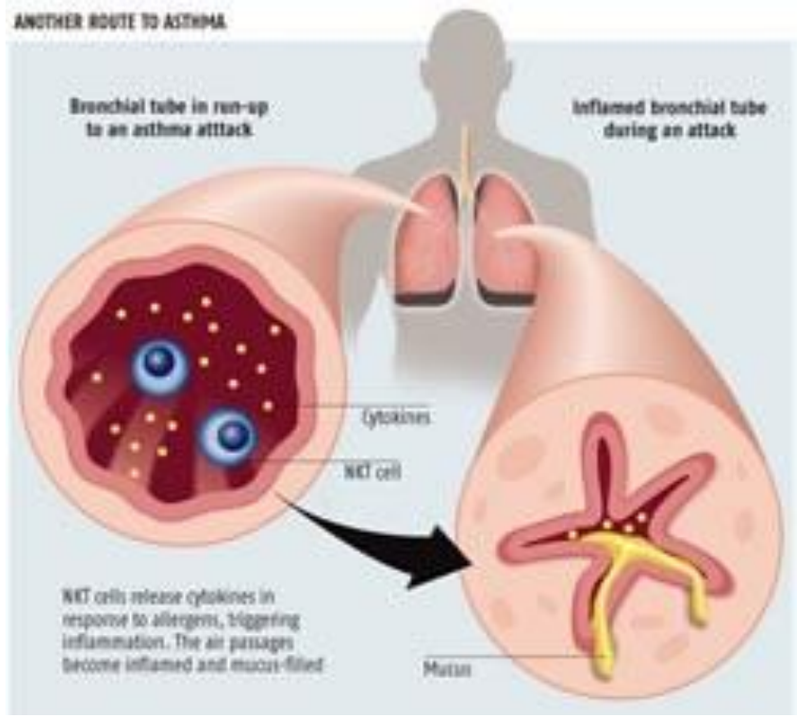
Matteo Bassetti[1*], Charles-Edouard Luyt[2,3], David P. Nicolau[4] and Jérôme Pugin[5]

Ann. Intensive Care (2016) 6:35



Efectos adversos

Tos y Broncoespasmo



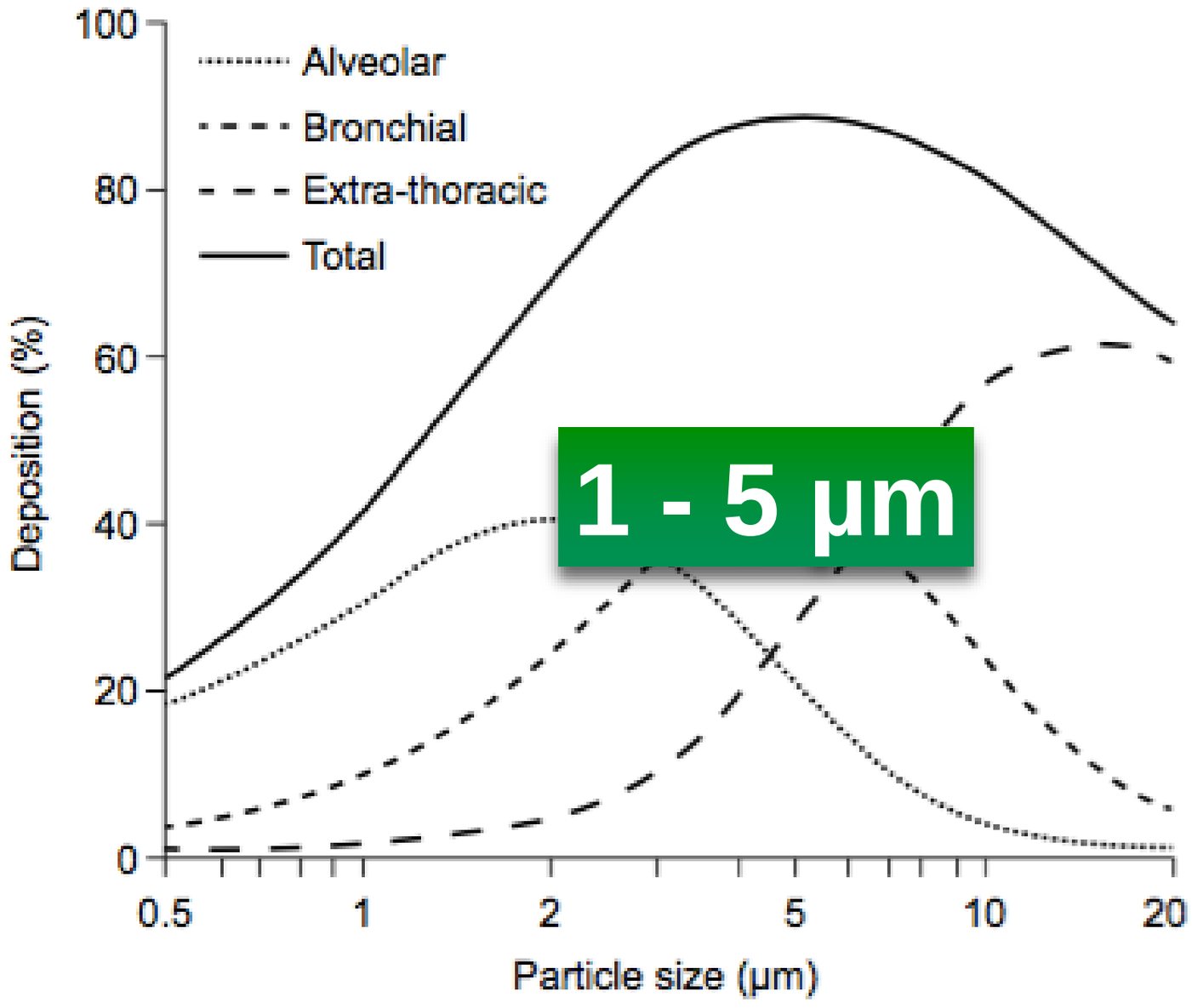
Disolución con agua de viales

Broncodilatadores previos?

Consensus summary of aerosolized antimicrobial agents: application of guideline criteria
Le J, Neuhauser M, Brown J, Gentry C, Klepser M, Marr A, Schiller D, Schwiesow J, Tice S, VandenBussche H, Wood C
Pharmacotherapy 2010;30:562-84

Aerosolized antibiotics for treating hospital-acquired and ventilator-associated pneumonia
Wood C
Exp Rev Enti-Infec Ther. 2011;9:993-1000

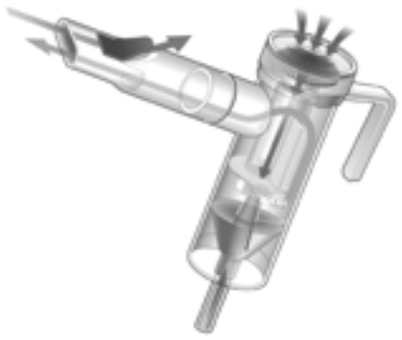
Características equipo nebulización

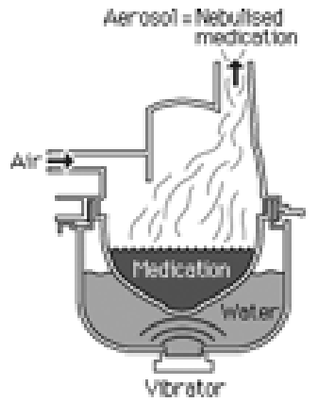


The influence of lung deposition on clinical response
Pritchard JN et al
Aerosol Med 2001;14(Suppl):19-26

Características equipo nebulización

Delivery systems	Advantages	Disadvantages
Jet nebulizer	Easy to use	Low drug delivery rate (15%)
	Low cost	Heterogeneously sized particles
		High gas flow requirement
		Generation of turbulent flow
		Difficult to clean
Ultrasonic nebulizer	Good drug delivery rate (30–40%)	Increases drug temperature
	No need for driving gas	Large residual volume
	Particle size ranging from 3.7 to 10.5 μm	Inability to aerosolize viscous solutions
	Silent	
Vibrating mesh nebulizer	Best drug delivery rate (40–60%)	Pores can clog
	Size of drug particle adjustable	Difficult to clean
	Low-velocity aerosol	High cost





Should Aerosolized Antibiotics Be Used to Treat Ventilator-Associated Pneumonia?
Zhang MD, Berra L, Klompas M
Respir Care 2016;61(6):737–748

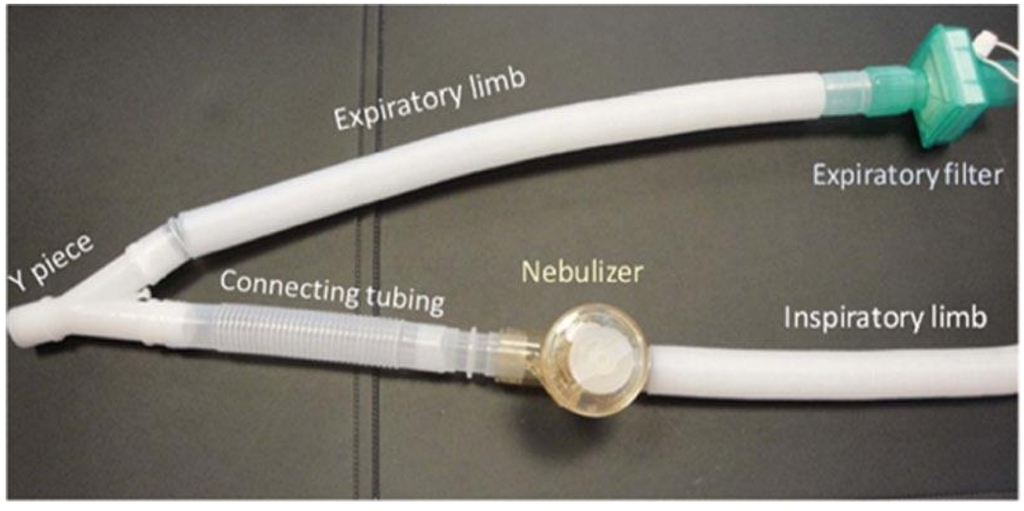
Parámetros ventilador

Mejor ventilación controlada por volumen

Sincronización con flujo inspiratorio

Volumen tidal > 500ml

Retirar humidificador



15 cm de la pieza Y en árbol inspiratorio

Delivering antibiotics to the lungs of patients with ventilator associated pneumonia: an update
Luyt CE, Brechot N, Combes A, Trouillet JL, Chastre J
Expert Rev. Anti Infect Ther 11(5), 511-521 (2013)

Aerosolized antibiotics for ventilator-associated pneumonia: lessons from experimental studies
LRouby JJ, Bouhemad B, Monsel A, Brisson H, Arbelot C, Lu Q
Anesthesiology. 2012;117:1364–80

Que dicen los estudios…

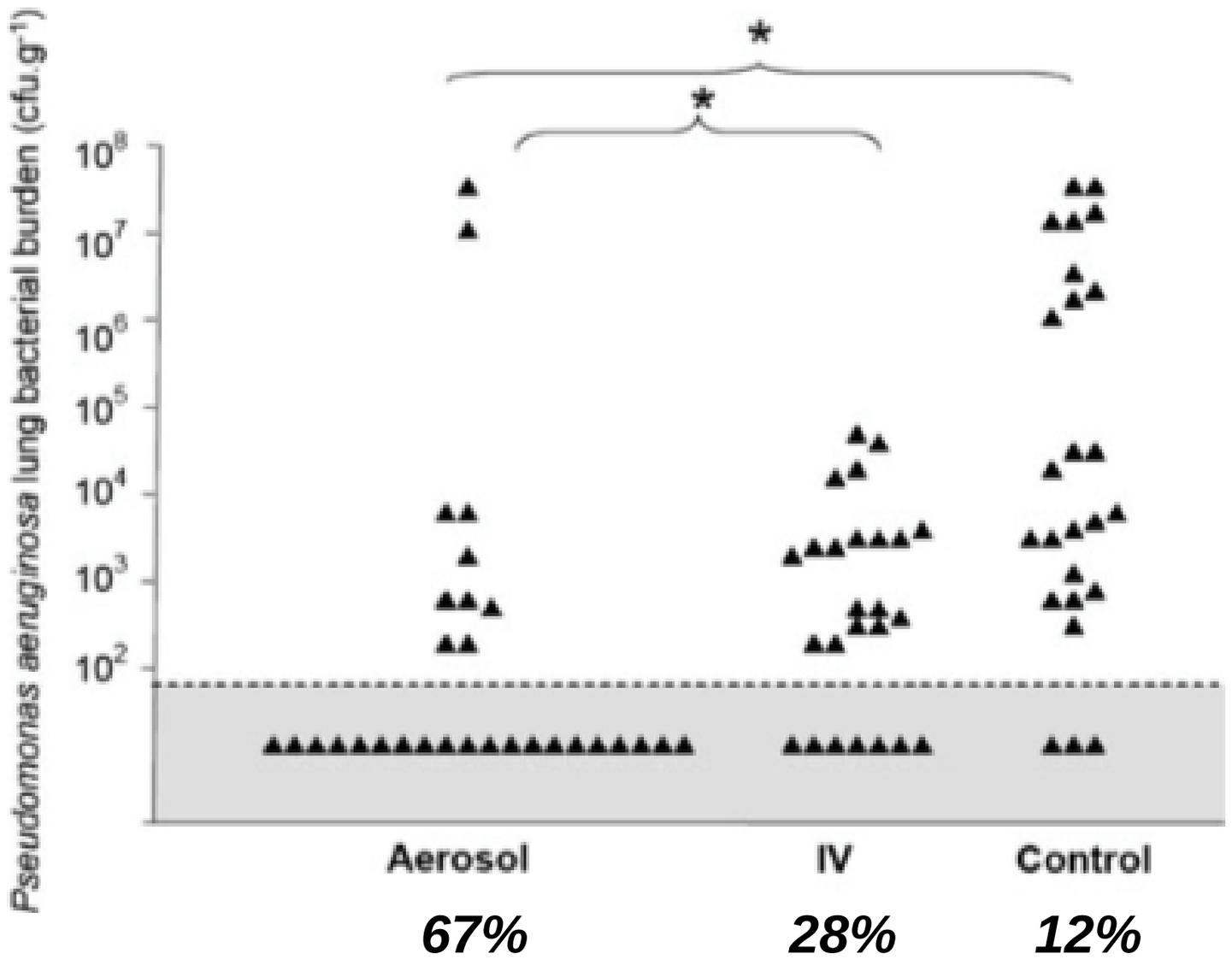
Intensive Care Med (2010) 36:1147–1155
DOI 10.1007/s00134-010-1879-4

ORIGINAL

Qin Lu
Cassio Girardi
Mao Zhang
Belaïd Bouhemad
Kamel Louchahi
Olivier Petitjean
Frédéric Wallet
Marie-Helene Becquemin
Gilles Le Naour
Charles-Hugo Marquette
Jean-Jacques Rouby

Nebulized and intravenous colistin in experimental pneumonia caused by *Pseudomonas aeruginosa*

6 piglets 40.000 UI/Kg c/8h iv
6 piglets 100.000 UI/Kg c/12h ih



Aerosolized antibiotics: do they add to the treatment of pneumonia?

Kollef M, Hamilton C, Montgomery B
Curr Opin Infect Dis December 2013, 26(6):538-544

Pobres metodologies, diferents nebulitzadors… Difícil comparar

Table 2. Recent clinical trials of aerosolized antibiotics in patients with ventilator-associated pneumonia

Reference	Design	Number of patients	Treatment	Outcomes (aerosol vs. control)
Arnold *et al.* [32▪▪]	Retrospective, single-center, cohort	93	Adjunct aerosolized colistin or tobramycin vs. intravenous antibiotics	30-day mortality: 0 vs. 18%
Lu *et al.* [19]	Prospective, randomized	40	Aerosolized ceftazidime and amikacin vs. intravenous ceftazidime and amikacin	Success: 70 vs. 55%; superinfection: 15 vs. 15%; day-28 mortality: 10 vs. 5%
Lu *et al.* [33▪▪]	Prospective, observational, comparative (not randomized)	165	Aerosolized colistin ± IV aminoglycosides vs. IV β-lactams plus aminoglycosides or quinolones	Clinical cure: 67 vs. 66%; superinfection: 6 vs. 13%; mortality: 16 vs. 23%
Niederman *et al.* [17▪▪]	Double blind, randomized	69	Aerosolized amikacin (q12 h, q24 h) or placebo, each with IV antibiotics	Target concentration: 50 vs. 17%; clinical cure: 94 vs. 75 vs. 88%
Montgomery *et al.* [26]	Double-blind, randomized, phase 1	4	Escalating doses of aerosolized amikacin and fosfomycin	Amikacin: ≥98-fold higher than *P. aeruginosa* MIC_{90}; fosfomycin: ≥68-fold higher than MRSA MIC_{90}

Inhaled colistin as adjunctive therapy to intravenous colistin for the treatment of microbiologically documented ventilator-associated pneumonia: a comparative cohort study

Clinical Microbiology and Infection, Volume 16 Number 8, August 2010

I. P. Korbila[1], A. Michalopoulos[1,2], P. I. Rafailidis[1,3], D. Nikita[4], G. Samonis[5] and M. E. Falagas[1,3,6]

	Colistin i.v. and inhaled (n = 78)	Colistin i.v. (n = 43)	p value
Treatment with additional active antibiotics	18/78 (23.1)	5/43 (11.6)	0.124
Intravenous colistin, days (mean ± SD)	16.9 ± 9.8	13.7 ± 11.2	**0.013**
Dosage of i.v. colistin, IU (mean ± SD)	(7.0 ± 2.4) × 10^6	(6.4 ± 2.3) × 10^6	0.13
Responsible pathogen, *n/N* (%)			
Acinetobacter baumannii	57/78 (73.1)	35/43 (81.4)	0.30
Pseudomonas aeruginosa	17/78 (21.8)	5/43 (11.6)	0.16
Klebsiella pneumoniae	4/78 (5.1)	3/43 (7)	0.68
Antimicrobial susceptibility, *n/N* (%)			
Polymyxin-only susceptible	37/78 (47.4)	31/43 (72.1)	**0.009**
Outcomes, *n/N* (%)			
Infection outcome (cure)	62/78 (79.5)	26/43 (60.5)	**0.025**
Mortality	31/78 (39.7)	19/43 (44.2)	0.63
ICU mortality	28/78 (35.9)	17/43 (39.5)	0.69

	Died (n = 50)	Survived (n = 71)	p value
Intravenous colistin, days (mean ± SD)	14.5 ± 8.5	16.7 ± 11.5	0.50
Dosage of i.v. colistin, IU (mean ± SD)	(5.9 ± 2.3) × 10^6	(7.4 ± 2.2) × 10^6	**0.001**
Responsible pathogen, *n/N* (%)			
Acinetobacter baumannii	34/50 (68)	58/71 (81.7)	0.08
Pseudomonas aeruginosa	13/50 (26)	9/71 (12.7)	0.06
Klebsiella pneumoniae	3/50 (6)	4/71 (5.6)	0.93
Antimicrobial susceptibility, *n/N* (%)			
Polymyxin-only susceptible	32/50 (64)	36/71 (50.7)	0.15
Outcomes, *n/N* (%)			
Infection outcome (cure)	17/50 (34)	71/71 (100)	**0.001**
Colistin use (i.v. plus inhaled)	31/50 (62)	47/71 (66.2)	0.64

CHEST

CHEST 2013; 144(6):1768–1775

Effect of Aerosolized Colistin as Adjunctive Treatment on the Outcomes of Microbiologically Documented Ventilator-Associated Pneumonia Caused by Colistin-Only Susceptible Gram-Negative Bacteria

Mario Tumbarello, MD; Gennaro De Pascale, MD; Enrico Maria Trecarichi, MD, PhD; Salvatore De Martino, MD; Giuseppe Bello, MD; Riccardo Maviglia, MD; Teresa Spanu, MD; and Massimo Antonelli, MD

	Treatment Cohorts[a]	
	AS-IV Colistin (n = 104)	IV Colistin (n = 104)

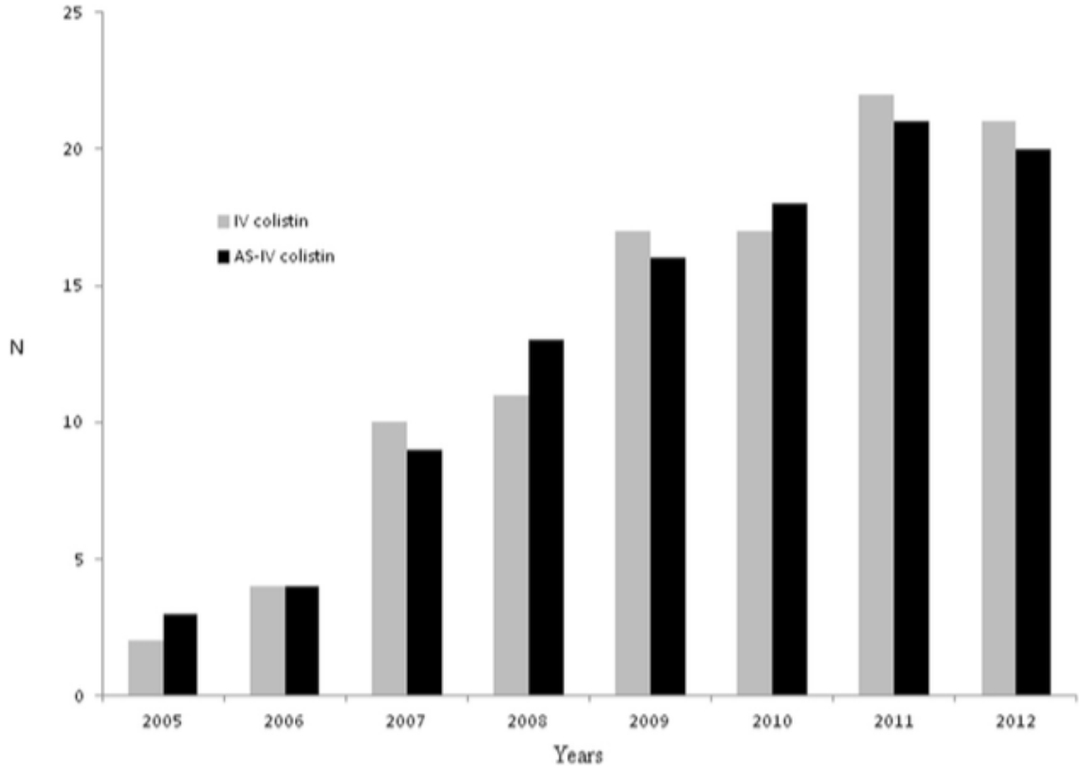


FIGURE 1. Temporal distribution of patients treated with IV colistin (IV cohort) and those who received IV and AS colistin (AS-IV cohort) in the study period. AS = aerosolized.

Table 3—*Multivariate Analysis of Factors Associated With Clinical Cure in Patients With VAP Caused by Colistin-Only Susceptible Gram-Negative Bacteria*

Variable	*P* Value	OR (95% CI)
Trauma-related ICU admission	.01	3.41 (1.27-9.14)
AS-IV colistin treatment	.009	2.58 (1.27-5.23)
SAPS II on admission	.002	0.96 (0.94-0.98)
SOFA score at VAP onset	.05	0.89 (0.80-0.99)
Septic shock at VAP onset	< .001	0.22 (0.11-0.47)
AKI onset during colistin treatment	.04	0.42 (0.19-0.95)

The Role of Aerosolized Colistin in the Treatment of Ventilator-Associated Pneumonia: A Systematic Review and Metaanalysis*

Crit Care Med. 2015;43:527–33

Antonis Valachis, MD, PhD[1]; George Samonis, MD, PhD[2]; Diamantis P. Kofteridis, MD, PhD[2]

Study or Subgroup	Adjunctive AS colistin Events	Total	IV colistin Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Doshi 2013	24	44	20	51	13.8%	1.86 [0.82, 4.21]
Kalin 2012	4	29	6	15	11.1%	0.24 [0.05, 1.05]
Kofteridis 2010	32	43	28	43	11.7%	1.56 [0.62, 3.94]
Korbila 2010	62	78	26	43	11.2%	2.53 [1.11, 5.76]
Naesens 2011	7	9	2	5	0.9%	5.25 [0.49, 56.80]
Pérez-Pedrero 2011	9	10	9	12	1.3%	3.00 [0.26, 34.57]
Rattanaumpawan 2010	26	51	26	49	21.2%	0.92 [0.42, 2.02]
Tumbarello 2013	72	104	57	104	28.7%	1.86 [1.05, 3.27]
Total (95% CI)		**368**		**322**	**100.0%**	**1.57 [1.14, 2.15]**
Total events	236		174			

Heterogeneity: Chi² = 11.05, df = 7 (P = 0.14); I² = 37%
Test for overall effect: Z = 2.77 (P = 0.006)

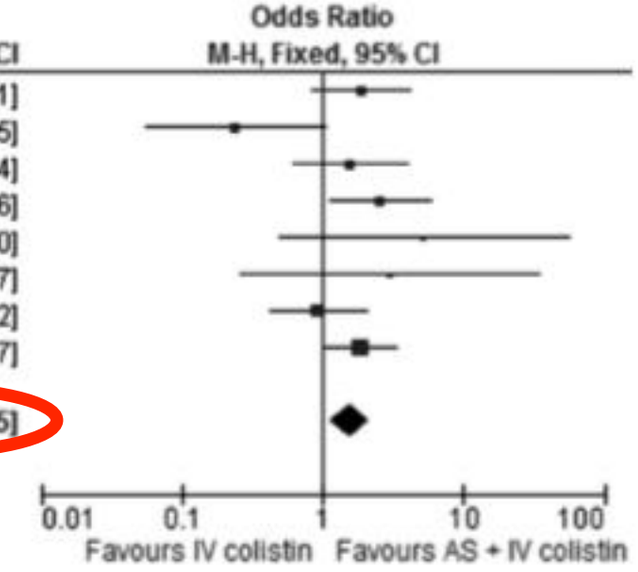


Figure 2. Forest plot of clinical response between patients who received aerosolized (AS) + IV colistin and those who received IV colistin.

Study or Subgroup	AS + IV colistin Events	Total	IV colistin Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Doshi 2013	15	44	27	51	17.8%	0.46 [0.20, 1.06]
Kalin 2012	16	29	7	15	4.5%	1.41 [0.40, 4.91]
Kofteridis 2010	10	43	18	43	14.9%	0.42 [0.17, 1.07]
Korbila 2010	31	78	19	43	16.0%	0.83 [0.39, 1.77]
Naesens 2011	3	9	5	5	4.8%	0.05 [0.00, 1.17]
Rattanaumpawan 2010	22	51	20	49	12.5%	1.10 [0.50, 2.44]
Tumbarello 2013	45	104	48	104	29.4%	0.89 [0.51, 1.54]
Total (95% CI)		**358**		**310**	**100.0%**	**0.74 [0.54, 1.01]**
Total events	142		144			

Heterogeneity: Chi² = 7.98, df = 6 (P = 0.24); I² = 25%
Test for overall effect: Z = 1.88 (P = 0.06)

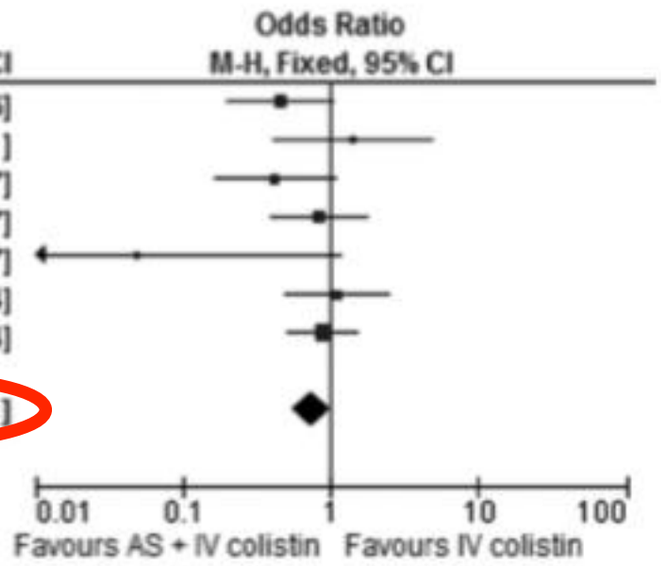


Figure 3. Forest plot of overall mortality between patients who received aerosolized (AS) + IV colistin and those who received IV colistin.

Nebulized antibiotics for ventilator-associated pneumonia: a systematic review and meta-analysis

Fernando G Zampieri[1,2,3*†], Antonio P Nassar Jr[1,2,4†], Dimitri Gusmao-Flores[1,5,6], Leandro U Taniguchi[2,7], Antoni Torres[8] and Otavio T Ranzani[1,8,9,10]

Critical Care (2015) 19:150

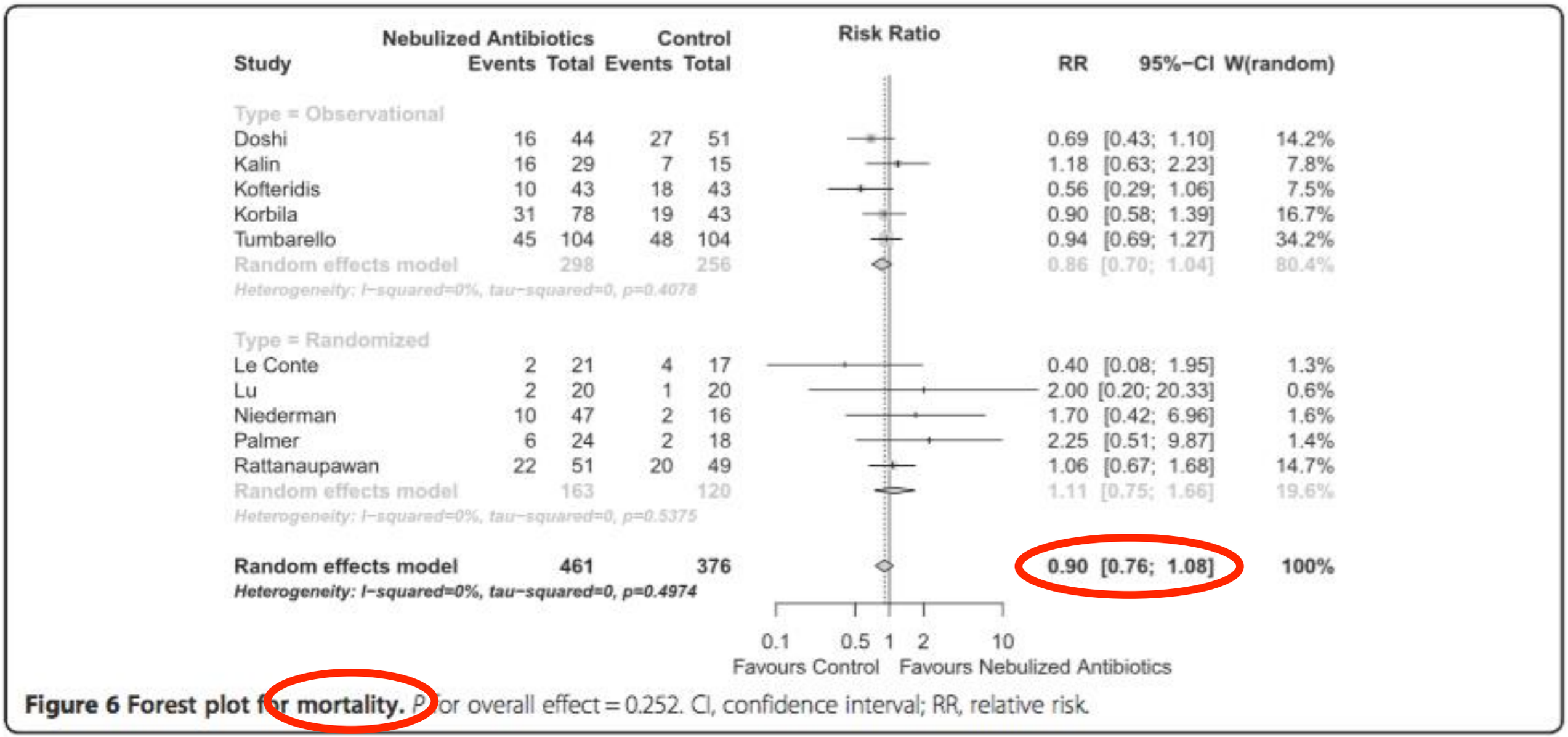


Figure 6 Forest plot for mortality. *P* for overall effect = 0.252. CI, confidence interval; RR, relative risk.

Nebulized antibiotics for ventilator-associated pneumonia: a systematic review and meta-analysis

Fernando G Zampieri[1,2,3*†], Antonio P Nassar Jr[1,2,4†], Dimitri Gusmao-Flores[1,5,6], Leandro U Taniguchi[2,7], Antoni Torres[8] and Otavio T Ranzani[1,8,9,10]

Critical Care (2015) 19:150

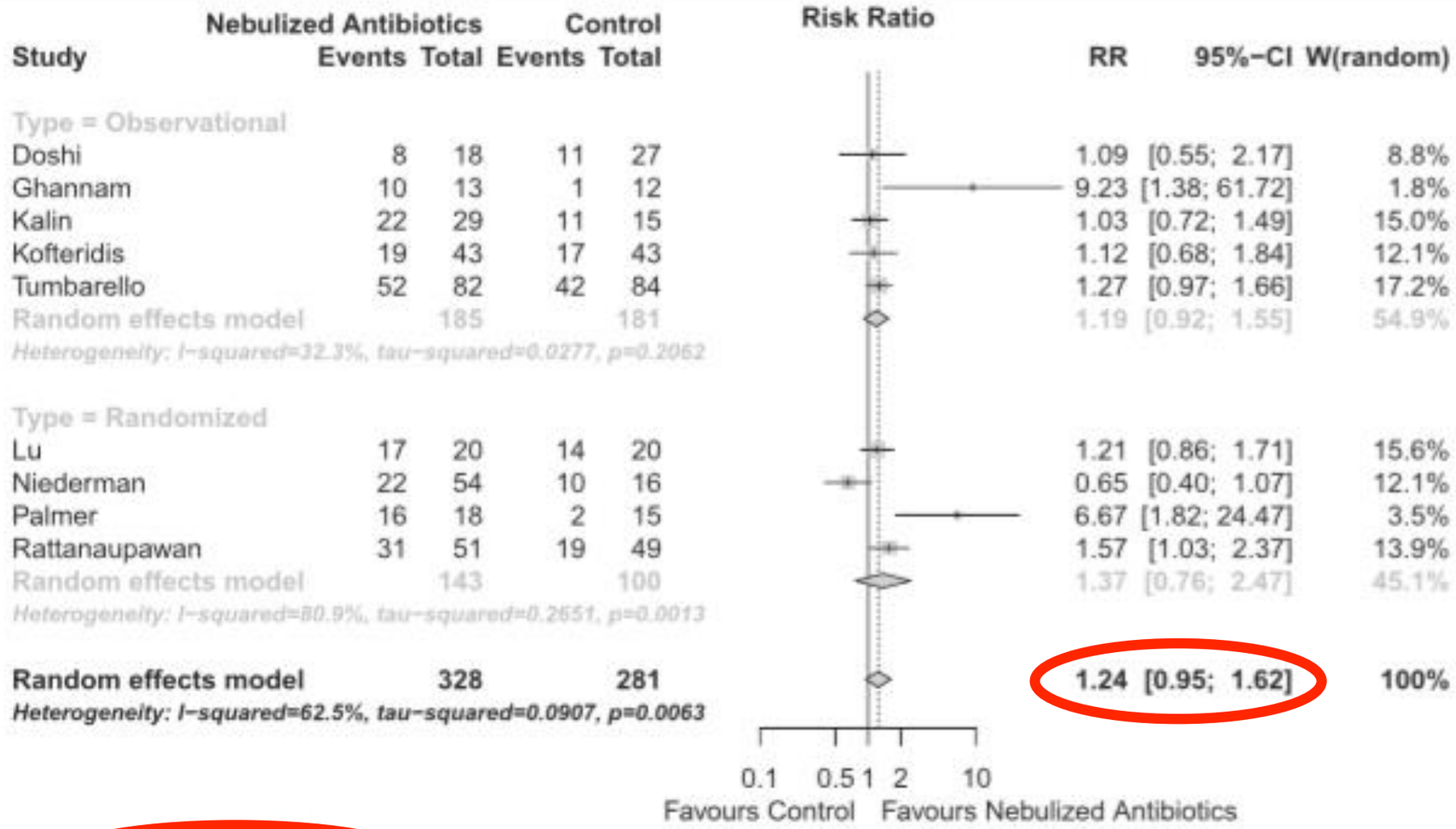


Figure 5 Forest plot for microbiological cure. for overall effect = 0.116. CI, confidence interval; RR, relative risk.

Nebulized antibiotics for ventilator-associated pneumonia: a systematic review and meta-analysis

Fernando G Zampieri[1,2,3*†], Antonio P Nassar Jr[1,2,4†], Dimitri Gusmao-Flores[1,5,6], Leandro U Taniguchi[2,7], Antoni Torres[8] and Otavio T Ranzani[1,8,9,10]

Critical Care (2015) 19:150

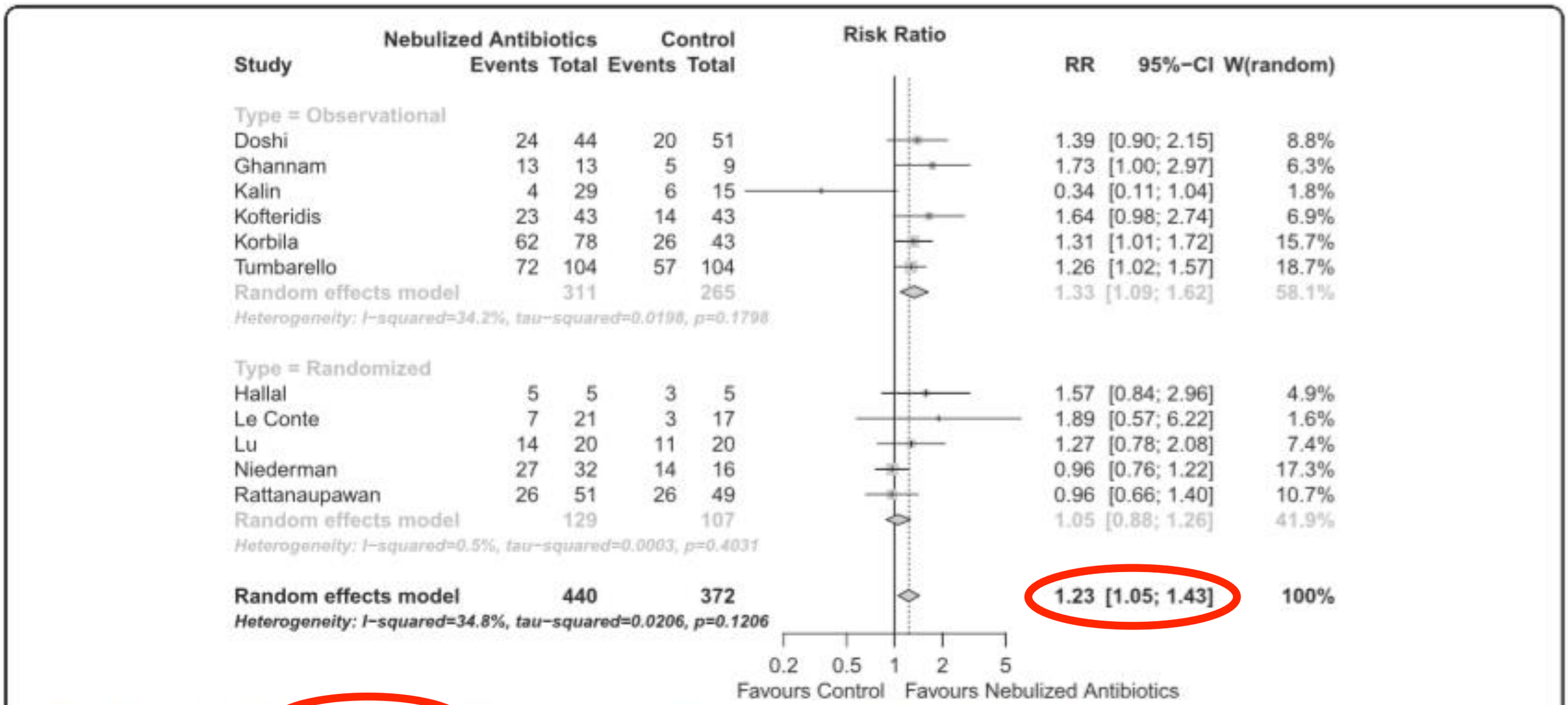


Figure 3 Forest plot for clinical cure. *P* for overall effect = 0.009. CI, confidence interval; RR, relative risk.

Honore *et al. Critical Care* (2015) 19:265
DOI 10.1186/s13054-015-0966-x

CRITICAL CARE

LETTER Open Access

Nebulized colistin for treatment of ventilator-associated pneumonia caused by multidrug-resistant Gram-negative bacteria: we still need to straighten out the dose!

Patrick M. Honore*, Rita Jacobs, Inne Hendrickx, Elisabeth De Waele, Jouke De Regt and Herbert D. Spapen

Gu *Critical Care* (2015) 19:236
DOI 10.1186/s13054-015-0952-3

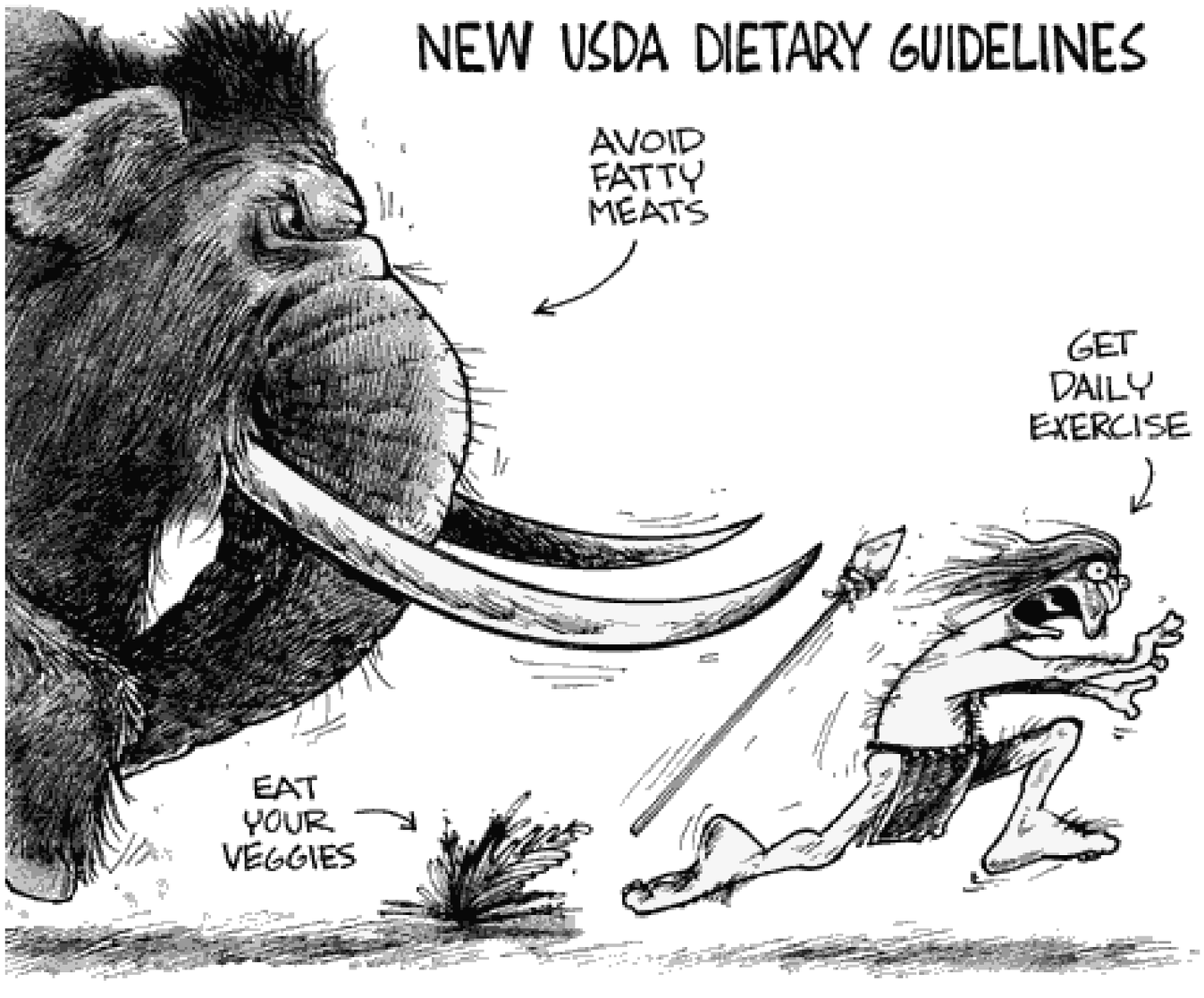
CRITICAL CARE

LETTER Open Access

Nebulized antibiotics for ventilator-associated pneumonia: misleading analysis and interpretation of the data

Wan-Jie Gu

Recomendaciones actuales



Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia

This official statement of the American Thoracic Society and the Infectious Diseases Society of America was approved by the ATS Board of Directors, December 2004 and the IDSA Guideline Committee, October 2004

Aerosolized antibiotics have not been proven to have value in the therapy of VAP (**Level I**) (256). However, they may be considered as adjunctive therapy in patients with MDR gram-negatives who are not responding to systemic therapy (**Level III**) (255).

Guies

AMMI CANADA GUIDELINES

Clinical practice guidelines for hospital-acquired pneumonia and ventilator-associated pneumonia in adults

C Rotstein, G Evans, A Born, et al. Clinical practice guidelines for hospital-acquired pneumonia and ventilator-associated pneumonia in adults. Can J Infect Dis Med Microbiol 2008;19(1):19-53.

Aerosolized antibiotics for VAP

Not all antibiotics achieve reasonable levels in the lung. Aerosolization of antibiotics allows greater access to the lower respiratory tract with higher levels being achieved in the ELF. Pseudomonal VAP unresponsive to systemically administered agents subsequently responded to aerosolized aminoglycosides or polymyxin, and aerosolized aminoglycosides have been used in cystic fibrosis patients for some time (234). Unfortunately, very few antibiotics have formulations developed specifically for administration by this route and often an intravenous formulation of a drug is used. Adverse effects such as bronchospasm may result when such an approach is tried. A nebulizer that delivers the appropriate particle size (1 μm to 5 μm) is also required. The use of aerosolized vancomycin may be worth exploring for treatment of MRSA HAP and VAP.

Realidad

Global survey on nebulization of antimicrobial agents in mechanically ventilated patients: a call for international guidelines

C. Solé-Lleonart[1,2], J. A. Roberts[3], J. Chastre[4], G. Poulakou[5], L. B. Palmer[6], S. Blot[7], T. Felton[8], M. Bassetti[9], C.-E. Luyt[4], J. M. Pereira[10], J. Riera[11], T. Welte[12], H. Qiu[13], J.-J. Rouby[14] and J. Rello[15], the ESGCIP Investigators

Clin Microbiol Infect 2016; **22:** 359–364

18 octubre 2014 - 31 enero 2015
192 ICUs - 87 para el análisis

TABLE 1. Indications for use of Neb including whether they are used in global (intravenous plus nebulized, or alone) or as sole (Neb alone) therapy/prophylaxis

	Asia (n = 37)		Europe (n = 32)		Australasia, North America and Latin America (n = 18)		Total (n = 87)	
Characteristic	Global, n (%)	Neb alone, n (%)	Global, n (%)	Neb alone, n (%)	Global, n (%)	Neb alone, n (%)	Global, n (%)	Neb alone, n (%)
VAP treatment	32 (86.4)	7 (18.9)	16 (50)	1 (9.3)	10 (55.5)	0 (0)	58 (66.6)	8 (9.1)
VAT treatment	31 (83.7)	9 (24.3)	19 (59.3)	9 (28.1)	6 (33.3)	2 (11.1)	56 (64.3)	20 (22.9)
Prophylaxis	25 (67.5)	16 (43.2)	10 (31.2)	9 (28.1)	9 (50)	1 (5.5)	44 (50.6)	26 (29.8)
MDRO treatment	28 (75.6)	6 (16.2)	27 (84.3)	3 (9.3)	12 (66.6)	0 (0)	67 (77)	9 (10.3)
MDRO colonization	23 (62.1)	10 (27.0)	17 (53.1)	11 (34.3)	6 (33.3)	1 (5.5)	46 (52.8)	22 (25.2)
Viral infection treatment	23 (62.1)	9 (24.3)	7 (21.8)	5 (15.6)	4 (22.2)	0 (0)	34 (39.1)	14 (16)
Fungal prophylaxis	25 (67.5)	8 (21.6)	7 (21.8)	6 (18.7)	9 (50)	3 (16.6)	41 (47.1)	17 (19.5)
Fungal treatment	21 (56.7)	6 (16.2)	8 (25)	4 (12.5)	3 (16.6)	0 (0)	32 (36.8)	10 (11.4)

IV, intravenous antibiotic therapy; MDRO, multidrug-resistant organism; Neb, nebulized antibiotic therapy; VAP, ventilator-associated pneumonia; VAT, ventilator-associated tracheobronchitis.

TABLE 2. Clinical indications used to guide prescription of nebulized antibiotics

Characteristic	Asia (n = 37), n (%)	Europe (n = 32), n (%)	Australasia, Latin America and North America (n = 18), n (%)	Total (n = 87), n (%)
Prophylaxis immunocompetent	5 (13.5)	1 (3.1)	0 (0)	6 (6.8)
Prophylaxis immunocompromised	12 (32.4)	7 (21.8)	4 (22.2)	23 (26.4)
Empirical treatment for increased pulmonary secretions	10 (27)	1 (3.1)	0 (0)	11 (12.6)
Empirical treatment for fever or leucocytosis	10 (27)	2 (6.2)	0 (0)	12 (13.7)
Empirical treatment for decreased $PaFiO_2$	5 (13.5)	0 (0)	0 (0)	5 (5.7)
Empirical treatment for pulmonary x-ray infiltrates	6 (16.2)	1 (3.1)	0 (0)	7 (8)
Positive pulmonary specimen cultures	10 (27)	8 (25)	4 (22.2)	22 (25.2)
Positive pulmonary specimen cultures with MDRO	20 (54)	30 (93.7)	12 (66.6)	62 (71.2)

MDRO, multidrug resistant organism.

TABLE 3. Types of antibiotics nebulized and reported frequency of use by geographic location

Antibiotic type	Asia (n = 37), n (%)	Europe (n = 32), n (%)	Australasia and North America (n = 18), n (%)	Total (n = 87), n (%)
Colistin base	4 (10.8)	11 (34.3)	9 (50)	24 (27.5)
CMS	0 (0)	30 (93.7)	6 (33.3)	36 (41.3)
Polymyxin B	2 (5.4)	2 (6.2)	1 (5.5)	5 (5.7)
Tobramycin	2 (5.4)	17 (19.4)	13 (72.2)	32 (36.7%)
Amikacin	7 (18.9)	9 (28.1)	7 (38.8)	23 (26.4)
Gentamicin	10 (27)	2 (6.2)	1 (5.5)	13 (14.9)
Netilmicin	0 (0)	0 (0)	0 (0)	0 (0)
Vancomycin	1 (2.7)	0 (0)	1 (5.5)	2 (2.3)
β-Lactams	0 (0)	2 (6.2)	0 (0)	2 (2.3)
Carbapenems	0 (0)	0 (0)	0 (0)	0 (0)
Macrolides	0 (0)	0 (0)	0 (0)	0 (0)
Aztreonam	0 (0)	0 (0)	3 (16.6)	3 (3.44)
Ribavirin	0 (0)	5 (15.6)	2 (11.1)	7 (8)
Pentamidine	0 (0)	4 (12.5)	6 (38.8)	10 (11.4)
Amphotericin B (prophylaxis)	2 (5.4)	4 (12.5)	3 (16.6)	9 (10.3)
Amphotericin B (treatment)	6 (16.2)	3 (9.3)	2 (11.1)	11 (12.6)
Other	1 (2.7)	2 (6.2)	2 (11.1)	5 (5.7)

CMS, colistin methanesulfonate.

A que dosis?

TABLE 4. Doses of nebulized colistin methanesulfonate prescribed for VAP and VAT

Dose	Asia (n = 37)		Europe (n = 32)		Australasia, Latin America and North America (n = 18)		Total (n = 87)	
	VAP, n (%)	VAT, n (%)	VAP, n (%)	VAT, n (%)	VAP, n (%)	VAT, n (%)	VAP, n (%)	VAT, n (%)
1 MIU/8 hours	1 (2.7)	3 (8.1)	5 (15.6)	7 (21.8)	2 (11.1)	1 (5.5)	8 (10.3)	11 (12.6)
2 MIU/8 hours	4 (10.8)	4 (36.3)	10 (31.5)	6 (18.7)	0 (0)	0 (0)	14 (16)	10 (11.4)
2 MIU/12 hours	1 (2.7)	3 (8.1)	5 (15.6)	4 (12.5)	1 (5.5)	1 (5.5)	7 (8)	8 (9.1)
3 MU/8 hours	2 (5.4)	1 (2.7)	7 (21.8)	4 (12.5)	2 (11.1)	1 (5.5)	11 (12.6)	6 (6.8)
5 MIU/12 hours	1 (2.7)	0 (0)	0 (0)	1 (3.1)	2 (11.1)	0 (0)	3 (3.4)	1 (1.1)
5 MIU/8 hours	2 (5.4)	0 (0)	3 (9.3)	0 (0)	0 (0)	0 (0)	5 (5.7)	0 (0)
Other dose	15 (40.5)	15 (40.5)	1 (3.1)	3 (9.3)	3 (16.6)	4 (22.2)	19 (21.8)	22 (25.2)

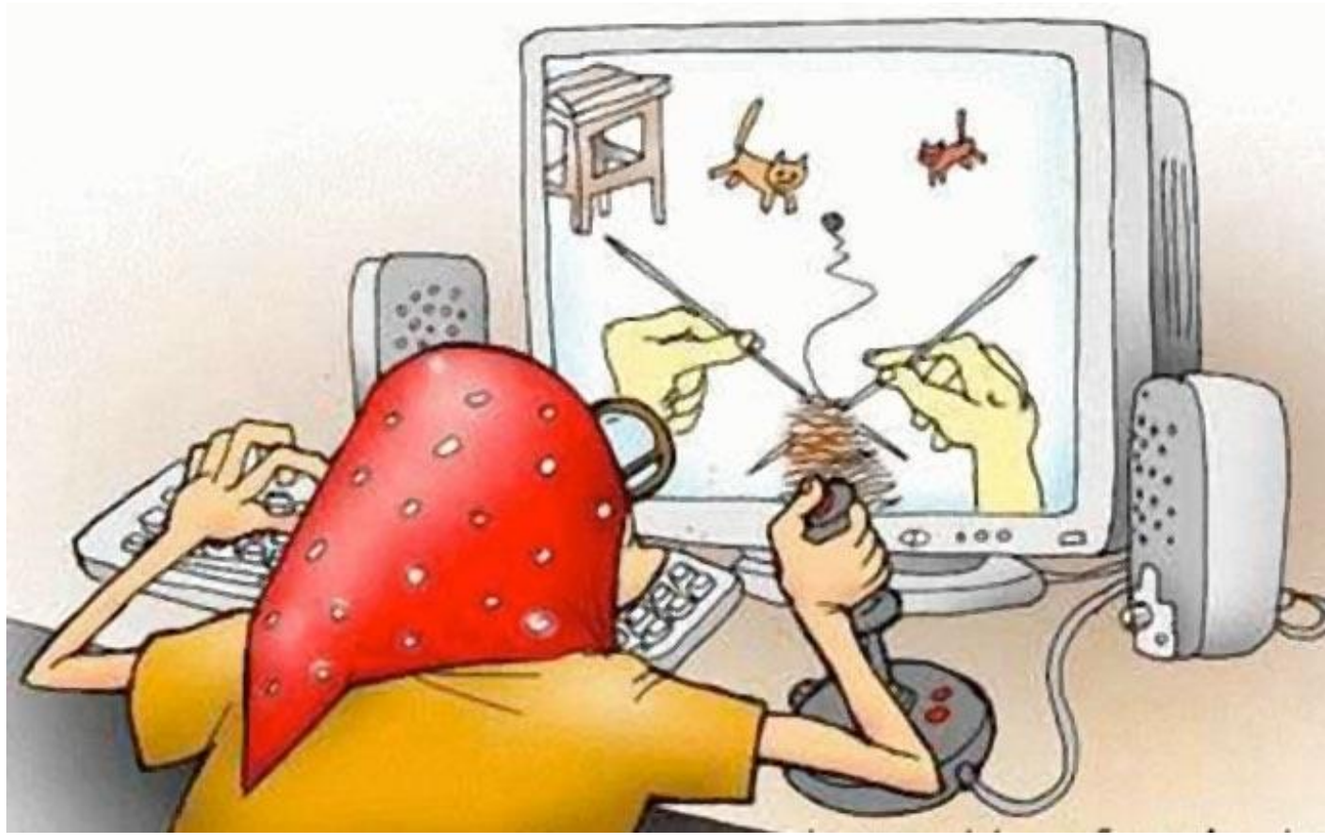
MIU, million international units; VAP, ventilator-associated pneumonia; VAT, ventilator-associated tracheobronchitis.

TABLE 5. Doses of nebulized tobramycin and amikacin prescribed for VAP and VAT

Dose	Asia (n = 37)		Europe (n = 32)		Australasia, Latin America and North America (n = 18)		Total (n = 87)	
	VAP, n (%)	VAT, n (%)	VAP, n (%)	VAT, n (%)	VAP, n (%)	VAT, n (%)	VAP, n (%)	VAT, n (%)
Tobramycin								
150 mg/12 hours	3 (8.1)	4 (10.8)	3 (9.3)	2 (6.2)	2 (11.1)	0 (0)	8 (9.1)	6 (6.8)
300 mg/24 hours	3 (8.1)	7 (18.9)	3 (9.3)	3 (9.3)	1 (5.5)	1 (5.5)	7 (8)	11 (12.6)
300 mg/12 hours	6 (16.2)	1 (2.7)	7 (21.8)	3 (9.3)	6 (33.3)	4 (22.2)	19 (21.8)	8 (9.1)
Other dose	14 (37.8)	14 (37.8)	1 (3.1)	2 (6.2)	2 (11.1)	3 (16.6)	17 (19.5)	19 (21.8)
Amikacin								
15 mg/kg/24 hours	3 (8.1)	7 (18.9)	1 (3.1)	2 (6.2)	1 (5.5)	0 (0)	5 (5.7)	9 (10.3)
15 mg/kg/12 hours	6 (16.2)	1 (2.7)	0 (0)	1 (3.1)	2 (11.1)	1 (5.5)	8 (9.1)	3 (3.4)
20 mg/kg/24 hours	3 (8.1)	5 (13.5)	3 (9.3)	1 (3.1)	1 (5.5)	1 (5.5)	7 (8)	7 (8)
20 mg/kg/12 hours	0 (0)	0 (0)	3 (9.3)	0 (0)	1 (5.5)	1 (5.5)	4 (4.5)	1 (1.1)
Other dose	3 (8.1)	12 (32.4)	3 (9.3)	3 (9.3)	4 (22.2)	4 (22.2)	10 (11.4)	19 (21.8)

VAP, ventilator-associated pneumonia; VAT, ventilator-associated tracheobronchitis.

Lo que vendrá…



Futuro

ClinicalTrials.gov NCT01969799

Aerosolized Amikacin and Fosfomycin in Mechanically Ventilated Patients With Gram-negative Pneumonia (IASIS)

To demonstrate the safety and efficacy of adjunctive therapy with the Amikacin fosfomycin inhalation system (AFIS) versus aerosolized placebo to treat Gram-negative pneumonia in mechanically ventilated patients receiving IV antibiotics.

Study Status:	This study has been completed.
Study Completion Date:	April 2016
Primary Completion Date:	March 2016 (Final data collection date for primary outcome measure)

Pharmacokinetics and lung delivery of PDDS-aerosolized amikacin (NKTR-061) in intubated and mechanically ventilated patients with nosocomial pneumonia

Charles-Edouard Luyt[1], Marc Clavel[2], Kalpalatha Guntupalli[3], Jay Johannigman[4], John I Kennedy[5], Christopher Wood[6], Kevin Corkery[7], Dennis Gribben[8] and Jean Chastre[1]

Safety and Tolerability of Nebulized Amoxicillin-Clavulanic Acid in Patients with COPD (STONAC 1 and STONAC 2)

COPD: JOURNAL OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE
2016, VOL. 0, NO. 0, 1–7

L.C. Nijdam[a], M.D.M. Assink[b], J.C. Kuijvenhoven[c], M.E.A. de Saegher[c], P.D.L.P.M. van der Valk[c], J. van der Palen[d,e], M.G.J. Brusse-Keizer[e], and K.L.L. Movig[a]

Optimization of nebulized delivery of linezolid, daptomycin, and vancomycin aerosol

Drug Design, Development and Therapy 2014:8

MP-376 (Aeroquin™, Levofloxacin for Inhalation) in Patients With Cystic Fibrosis


"Winter
is coming"

Lluís Campins i Bernadàs
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