Olgu Eşliğinde
Dirençli Gram Pozitif Kok Enfeksiyonlarının Tedavisi

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Dirençli Gram Pozitif Bakteriler

- ✓ MRSA, VISA, h-VISA
- ✓ VRE
- ✓ Pnömokok

Olgu 1
KK, 73 y, E

- ✓ DM, HT, KBY, KOAH
- ✓ Kateter yerleştirilmesi sırasında gelişen hematom & 4 st sonra kardiyak arrest
- ✓ 40 dk KPR, Entübasyon, 48 saat YBÜ yatış
- ✓ YBÜ'den 5 gün sonra gelişen Acinetobacter pnömonisi
- ✓ Denenen farklı kombinasyonlara yanıtsız
- ✓ Bir gün farklı hastanede izlem sonrası devir alındı

- ✓ Hemodiyafiltrasyon + Mekanik ventilasyon
  - Kolistin (23.4.2016)
  - 25-27.4.2016 Tigesiklin → Direnç gelişimi
  - + teikoplanin 600 mg (28.4.2016) başlandı
- ✓ Kabulünde alınan ETA kültürü
  - Saf ve bol miktarda MRSA
- ✓ Teikoplanin devam mı?
- ✓ Linezolide geçelim mi?

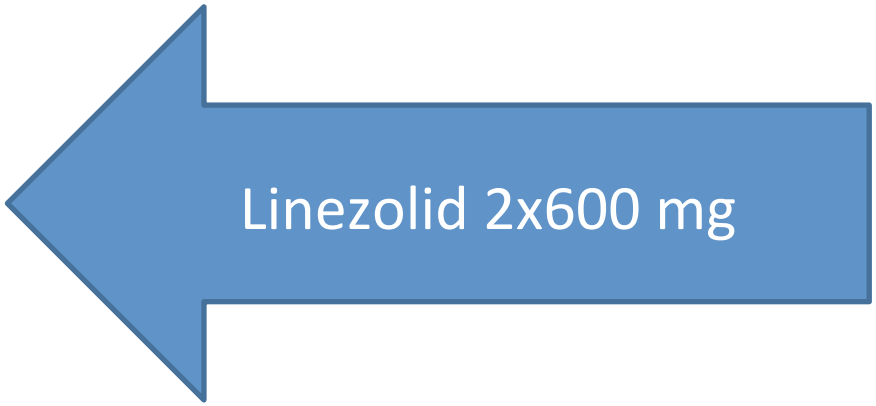
Klinik Yanıt çok iyi:
3. Gün sonunda «easy-breath»
4. Gün ekstübe oldu
50 ml/st idrar başladı
8. Gün hemofiltrasyon kesildi
Kreatinin 1.44
Antibiyotik doz ayarı
Kolistin 1x100
Teiko q 48 st

Bir gün sonra….
6/5/2016

- ✓ Vücut ısısı 37.8
- ✓ Oksijenasyon bozuldu; CO2 retansiyonu; renal fonksiyonlar geriledi
- ✓ Sekresyonları çok arttı
  - 10^5 cfu/ml MRSA + az miktarda maya (C. albicans)

Neden??

- ✓ Yeni bir enfeksiyon?
  - Candida??
- ✓ Renal fonksiyon değişikliği-doz ayarı
  - 48 saat ara
- ✓ Farmakokinetik ?
  - 10 mg/kg
- ✓ hVISA



4 gün sonra….

- 6.5.16’da alınan kan kültürlerinde de **MRSA**
  - **Vanko MİK 2mcg/ml**
  - **Teiko MİK 4 mcg/ml**

Uygun Tedavinin Önemi

- MSSA İle enfekte hastaların **%21**'i, MRSA ile enfekte hastaların ise **%52'**si uygunsuz ampirik tedavi almaktadır.
- Uygun antibiyotik başlanması için geçen süre ortalama 10 gün uzamaktadır

	Bakteremi (n=152)	DYDE (n=132)	FN (n=190)	Endokardit (n=90)	i.v. kateter (n=31)	Toplam (n=605)
İlk basamakta anti-MRSA alamayan, %	45	49	58	49	44	49
İkinci basamakta anti-MRSA alması için geçen süre (gün)	6	10	13	5	5	6
Üçüncü basamakta anti-MRSA alması için geçen süre (gün)	6	17	5	15	6	8

Referans:
1. Ammerlaan H et al. ISCVID 2007

Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections in Adults and Children

Catherine Liu,[1] Arnold Bayer,[3,5] Sara E. Cosgrove,[6] Robert S. Daum,[7] Scott K. Fridkin,[8] Rachel J. Gorwitz,[9] Sheldon L. Kaplan,[10] Adolf W. Karchmer,[11] Donald P. Levine,[12] Barbara E. Murray,[14] Michael J. Rybak,[12,13] David A. Talan,[4,5] and Henry F. Chambers[1,2]

• CID 2011:52 (1 February)

IV. What is the management of MRSA pneumonia?

Pneumonia

32. For hospitalized patients with severe community-acquired pneumonia defined by any one of the following: (1) a requirement for intensive care unit (ICU) admission, (2) necrotizing or cavitary infiltrates, or (3) empyema, empirical therapy for MRSA is recommended pending sputum and/or blood culture results (A-III).

33. For health care–associated MRSA (HA-MRSA) or CA-MRSA pneumonia, IV vancomycin (A-II) or linezolid 600 mg PO/IV twice daily (A-II) or clindamycin 600 mg PO/IV 3 times daily (B-III), if the strain is susceptible, is recommended for 7–21 days, depending on the extent of infection.

34. In patients with MRSA pneumonia complicated by empyema, antimicrobial therapy against MRSA should be used in conjunction with drainage procedures (A-III).

Table 3. Recommendations for the Treatment of Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Manifestation	Treatment	Adult dose	Pediatric dose	Class[a]	Comment
Skin and soft-tissue infection (SSTI)					
Abscess, furuncles, carbuncles	Incision and drainage			AII	For simple abscesses or boils, incision and drainage is likely adequate. Please refer to Table 2 for conditions in which antimicrobial therapy is recommended after incision and drainage of an abscess due to CA-MRSA.
Purulent cellulitis (defined as cellulitis associated with purulent drainage or exudate in the absence of a drainable abscess)	Clindamycin	300–450 mg PO TID	10–13 mg/kg/dose PO every 6–8 h, not to exceed 40 mg/kg/day	AII	*Clostridium difficile*–associated disease may occur more frequently, compared with other oral agents.
	TMP-SMX	1–2 DS tab PO BID	Trimethoprim 4–6 mg/kg/dose, sulfamethoxazole 20–30 mg/kg/dose PO every 12 h	AII	TMP-SMX is pregnancy category C/D and not recommended for women in the third trimester of pregnancy and for children <2 months of age.
	Doxycycline	100 mg PO BID	≤45kg: 2 mg/kg/dose PO every 12 h >45kg: adult dose	AII	Tetracyclines are not recommended for children under 8 years of age and are pregnancy category D.
	Minocycline	200 mg × 1, then 100 mg PO BID	4 mg/kg PO × 1, then 2 mg/kg/dose PO every 12 h	AII	
	Linezolid	600 mg PO BID	10 mg/kg/dose PO every 8 h, not to exceed 600 mg/dose	AII	More expensive compared with other alternatives
Nonpurulent cellulitis (defined as cellulitis with no purulent drainage or exudate and no associated abscess)	β-lactam (eg, cephalexin and dicloxacillin)	500 mg PO QID	Please refer to Red Book	AII	Empirical therapy for β-hemolytic streptococci is recommended (AII). Empirical coverage for CA-MRSA is recommended in patients who do not respond to β-lactam therapy and may be considered in those with systemic toxicity.
	Clindamycin	300–450 mg PO TID	10–13 mg/kg/dose PO every 6–8 h, not to exceed 40 mg/kg/day	AII	Provide coverage for both β-hemolytic streptococci and CA-MRSA
	β-lactam (eg, amoxicillin) and/or TMP-SMX or a tetracycline	Amoxicillin: 500 PO mg TID See above for TMP-SMX and tetracycline dosing	Please refer to Red Book See above for TMP-SMX and tetracycline dosing	AII	Provide coverage for both β-hemolytic streptococci and CA-MRSA
	Linezolid	600 mg PO BID	10 mg/kg/dose PO every 8 h, not to exceed 600 mg/dose	AII	

Table 3. (*Continued*)

Manifestation	Treatment	Adult dose	Pediatric dose	Class[a]	Comment
					Provide coverage for both β-hemolytic streptococci and CA-MRSA
Complicated SSTI	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	AI/AII	
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	AI/AII	For children ≥12 years of age, 600 mg PO/IV BID. Pregnancy category C
	Daptomycin	4 mg/kg/dose IV QD	Ongoing study	AI/ND	The doses under study in children are 5 mg/kg (ages 12–17 years), 7 mg/kg (ages 7–11 years), 9 mg/kg (ages 2–6 years) (Clinicaltrials.gov NCT 00711802). Pregnancy category B.
	Telavancin	10 mg/kg/dose IV QD	ND	AI/ND	Pregnancy category C
	Clindamycin	600 mg PO/IV TID	10–13 mg/kg/dose PO/IV every 6–8 h, not to exceed 40 mg/kg/day	AII/AII	Pregnancy category B
Bacteremia and infective endocarditis					
Bacteremia	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	AII	The addition of gentamicin (AII) or rifampin (AII) to vancomycin is not routinely recommended.
	Daptomycin	6 mg/kg/dose IV QD	6–10 mg/kg/dose IV QD	AI/CIII	For adult patients, some experts recommend higher dosages of 8–10 mg/kg/dose IV QD (BIII). Pregnancy category B.
Infective endocarditis, native valve	Same as for bacteremia				
Infective endocarditis, prosthetic valve	Vancomycin and gentamicin and rifampin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BIII	
		1 mg/kg/dose IV every 8 h	1 mg/kg/dose IV every 8 h		
		300 mg PO/IV every 8 h	5 mg/kg/dose PO/IV every 8 h		
Persistent bacteremia	Please see text				
Pneumonia					
	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	AII	
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	AII	For children ≥12 years, 600 mg PO/IV BID. Pregnancy category C.
	Clindamycin	600 mg PO/IV TID	10–13 mg/kg/dose PO/IV every 6–8 h, not to exceed 40 mg/kg/day	BII/AII	Pregnancy category B.

Table 3. (Continued)

Manifestation	Treatment	Adult dose	Pediatric dose	Class[a]	Comment
Bone and joint infections					
Osteomyelitis	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII/AII	Surgical debridement and drainage of associated soft-tissue abscesses is the mainstay of therapy. (AIII). Some experts recommend the addition of rifampin 600 mg QD or 300–450 mg BID to the chosen antibiotic (BIII). For children ≥12 years of age, linezolid 600 mg PO/IV BID should be used. A single-strength and DS tablet of TMP-SMX contains 80 mg and 160 mg of TMP, respectively. For an 80-kg adult, 2 DS tablets achieves a dose of 4 mg/kg.
	Daptomycin	6 mg/kg/day IV QD	6–10 mg/kg/day IV QD	BII/CIII	
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII/CIII	
	Clindamycin	600 mg PO/IV TID	10–13 mg/kg/dose PO/IV every 6–8 h, not to exceed 40 mg/kg/day	BII/AII	
	TMP-SMX and rifampin	3.5–4.0 mg/kg/dose PO/IV every 8–12 h	ND	BII/ND	
		600 mg PO QD			
Septic arthritis	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII/AII	Drainage or debridement of the joint space should always be performed (AII).
	Daptomycin	6 mg/kg/day IV QD	6–10 mg/kg/dose IV QD	BII/CIII	
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII/CIII	
	Clindamycin	600 mg PO/IV TID	10–13 mg/kg/dose PO/IV every 6–8 h, not to exceed 40 mg/kg/day	BII/AII	
	TMP-SMX	3.5–4.0 mg/kg/dose PO/IV every 8–12 h	ND	BII/ND	
Prosthetic joint, spinal implant infections	Please see text				
Central nervous system infections					

Table 3. (Continued)

Manifestation	Treatment	Adult dose	Pediatric dose	Class[a]	Comment
Meningitis	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII	Some experts recommend the addition of rifampin 600 mg QD or 300–450 mg BID to vancomycin for adult patients (BIII). For children ≥12 years of age, linezolid 600 mg BID.
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII	
	TMP-SMX	5 mg/kg/dose PO/IV every 8-12 h	ND	CIII/ND	
Brain abscess, subdural empyema, spinal epidural abscess	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII	Some experts recommend the addition of rifampin 600 mg QD or 300–450 mg BID to vancomycin for adult patients (BIII). For children ≥12 years of age, linezolid 600 mg BID.
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII	
	TMP-SMX	5 mg/kg/dose PO/IV every 8–12 h	ND	CIII/ND	
Septic thrombosis of cavernous or dural venous sinus	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII	Some experts recommend the addition of rifampin 600 mg QD or 300–450 mg BID to vancomycin for adult patients (BIII). For children ≥12 years of age, linezolid 600 mg BID
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII	
	TMP-SMX	5 mg/kg/dose PO/IV every 8-12 h	ND	CIII/ND	

NOTE. BID, twice daily; CA-MRSA, community-associated MRSA; DS, double strength; IV, intravenous; ND, no data; PO, oral; QD, every day; TID, 3 times per day; TMP-SMX, trimethoprim-sulfamethoxazole.

[a] Classification of the strength of recommendation and quality of evidence applies to adult and pediatric patients unless otherwise specified. A backslash (/) followed by the recommendation strength and evidence grade will denote any differences in pediatric classification.

YBÜ Hastasında Teikoplanin Dozu Ne Olmalı?

- ✓ S.aureus sepsis-Retrospektif-80 hasta
  - Yanıt alınanlarda doz öncesi serum kons ve verilen doz yüksek
  - Yaşlıda idame düzey >10mg/l ise tedavi başarısı >90

Harding, et al. JAC 2000

- ✓ 6 mg/kg/gün dozunda idame düzey 7-10 mg/L

Whitehouse, et al. JAC 2005

- ✓ Lösemi hastalarında 120. saatte 5/11 hastada >10 mg/L

Pea, et al. Clin Pharmacokinet 2004

Intensive Care Med (2006) 32:775–779
DOI 10.1007/s00134-006-0136-3

BRIEF REPORT

Olivier Mimoz
Delphine Rolland
Michèle Adoun
Sandrine Marchand
Dominique Breilh
Ivan Brumpt
Bertrand Debaene
William Couet

Steady-state trough serum and epithelial lining fluid concentrations of teicoplanin 12 mg/kg per day in p[illegible]ents with ventilator-associated pneumoni[illegible]

Pnömoni dozu en az 12mg/kg olmalı !

Patient no.	Total				
1	20.1	4			
2	10.1	3.4			
3	8.8	3.7			
4	13.8	2.8	20	3.6	128
5	15.0	4.6	31	11.8	256
6	13.5	3.0	22	2.0	66
7	15.9	4.5	28	10.8	240
8	16.2	5.4	33	2.6	48
9	21.0	4.6	22	5.4	117
10	18.1	4.3	24	5.6	130
11	23.8	2.0	8	4.9	245
12	29.9	2.6	9	3.8	146
13	14.2	2.4	17	3.5	146
Median	15.9	3.7	22	4.9	146
Range	8.8–29.9	2.0–5.4	8–42	2.0–11.8	48–332

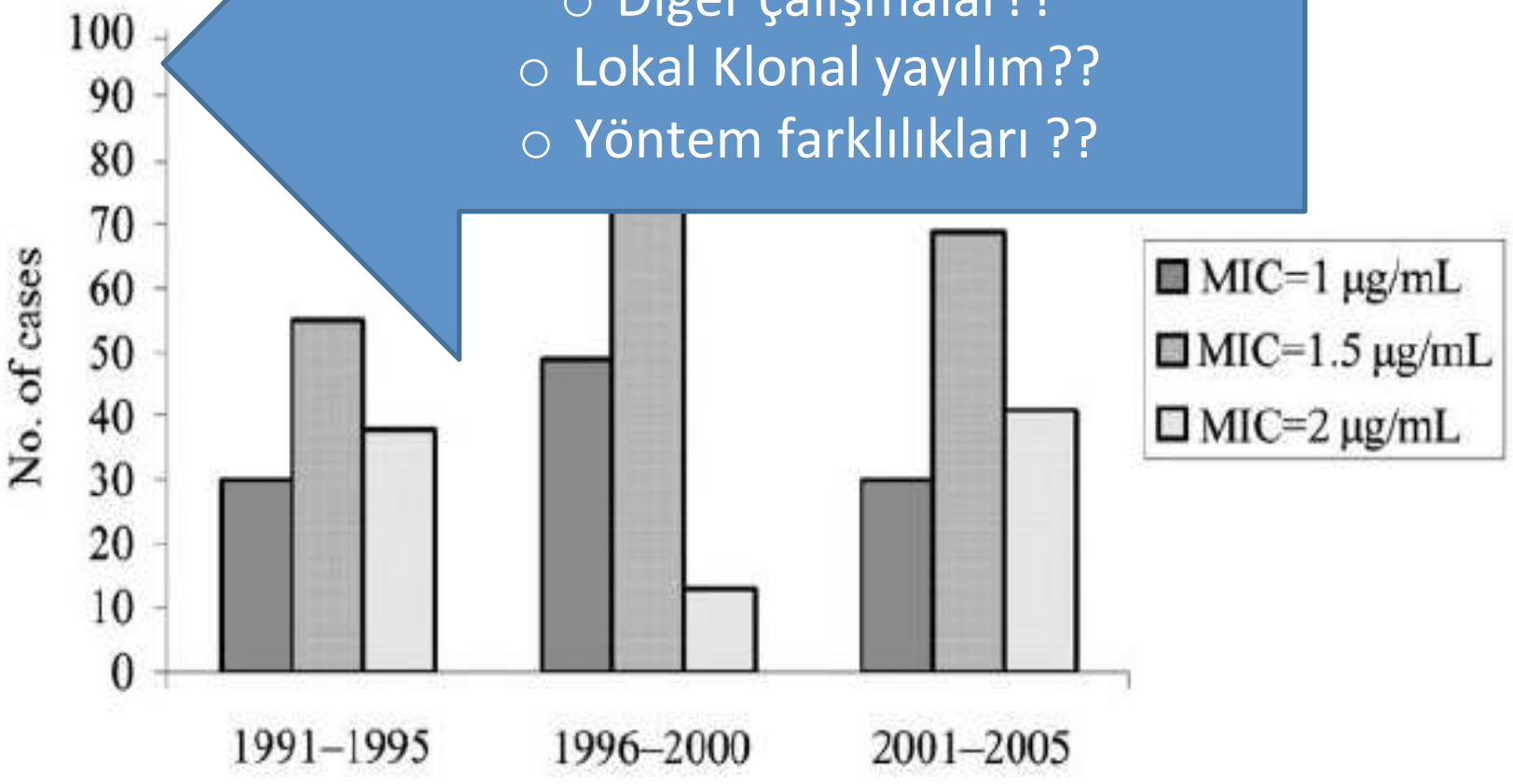
Mimoz O, et al. Intensive Care Med (2006) 32:775–779

Vankomisin

- ✓ 15-20 mg/kg/doz 8-12 st ara ile
- ✓ Ciddi hastalarda yükleme dozu (25-30 mg/kg)
  - Sepsis
  - Menenjit
  - Pnömoni
  - İnfektif Endokardit
- ✓ Düzey takibi
  - 4-5.doz arasında idame düzey
    - Ciddi hasta
    - Morbid obez
    - Renal fonk boz ve hemodiyaliz
    - VD flukyuasyonları

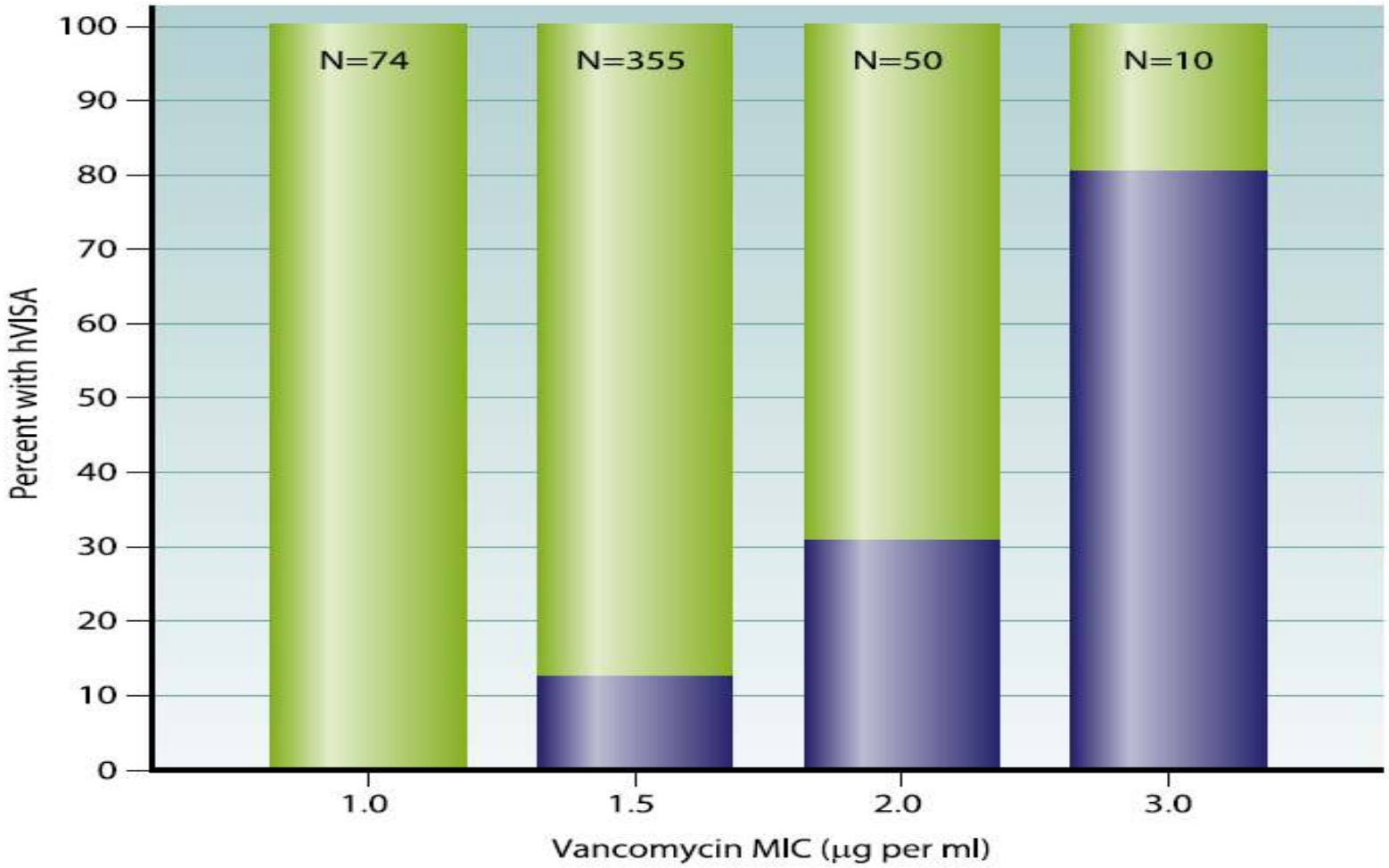
MİK kayması

- Diğer çalışmalar??
- Lokal Klonal yayılım??
- Yöntem farklılıkları ??



Soriano, CID 2008;46:193-200

MİK / hVISA



Musta AC, JCM 2009;47:1640

Yüksek MİK - tedavi başarısızlığı

TABLE 1. Comparison of outcomes between high (≥1.5 mg/liter) and low (<1.5 mg/liter) vancomycin MICs

Outcome	High MIC (n = 66)	Low MIC (n = 26)	P value
Overall failure[a]	24 (36.4)	4 (15.4)	0.049
30-day mortality[a]	12 (18.2)	3 (11.5)	0.5
Microbiologic failure[a]	6 (9.1)	0 (0)	0.18
Recurrence within 60 days[a]	11 (16.7)	1 (3.8)	0.17
Hospital length of stay after blood culture collection, median (IQR)	21 (9.0–43.0)	10.5 (9.0–16.5)	0.02
Switched to alternative antibiotic[a]	13 (19.7)	2 (7.7)	0.21

Lodise TP, AAC 2008;52:3315-20

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Jan. 2011, p. 405–410 Vol. 55, No. 1
0066-4804/11/$12.00 doi:10.1128/AAC.01133-10

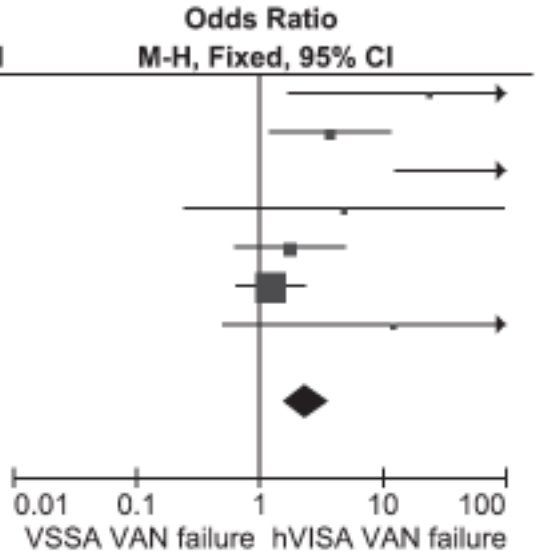
Systematic Review and Meta-Analysis of the Significance of Heterogeneous Vancomycin-Intermediate *Staphylococcus aureus* Isolates[▽]

Sebastiaan J. van Hal[1]* and David L. Paterson[2]

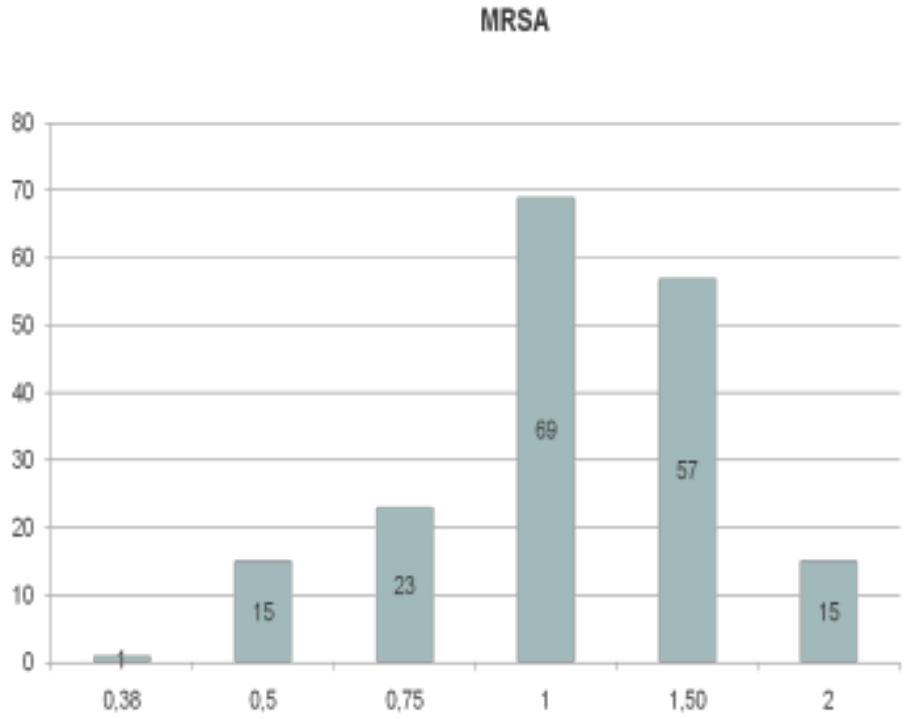
Department of Microbiology and Infectious Diseases, Liverpool Hospital, Liverpool BC, NSW 1087, Sydney, Australia,[1] and University of Queensland Centre for Clinical Research, Royal Brisbane and Women's Hospital Campus, Herston, QLD 4029, Australia[2]

Study or Subgroup	hVISA Events	hVISA Total	VSSA Events	VSSA Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Ariza (2)	12	14	1	5	0.8%	24.00 [1.69, 340.99]
Bae et al (4)	13	19	17	46	12.2%	3.70 [1.18, 11.53]
Charles et al (8)	5	5	1	48	0.1%	348.33 [12.59, 9636.20]
Fong et al (16)*	9	9	21	26	2.3%	4.86 [0.24, 97.05]
Horne et al (24)	10	26	11	42	20.2%	1.76 [0.62, 5.02]
Musta et al (41)	20	43	101	242	63.5%	1.21 [0.63, 2.33]
Neoh et al (42)	2	2	5	18	1.0%	12.27 [0.50, 299.32]
Total (95% CI)		**118**		**427**	**100.0%**	**2.37 [1.53, 3.67]**
Total events	71		157			

Heterogeneity: Chi² = 17.79, df = 6 (P = 0.007); I² = 66%
Test for overall effect: Z = 3.88 (P = 0.0001)



MRSA MİK dağılımı



	MRSA N:180 (%)
MİK ≤ 1 mg/L	108 (%60)
MİK= 1,5 mg/L	57 (%32)
MİK = 2 mg/L	15 (%8)

Tigen-Tükenmez E, 9. FEN Simpozyumu, P34

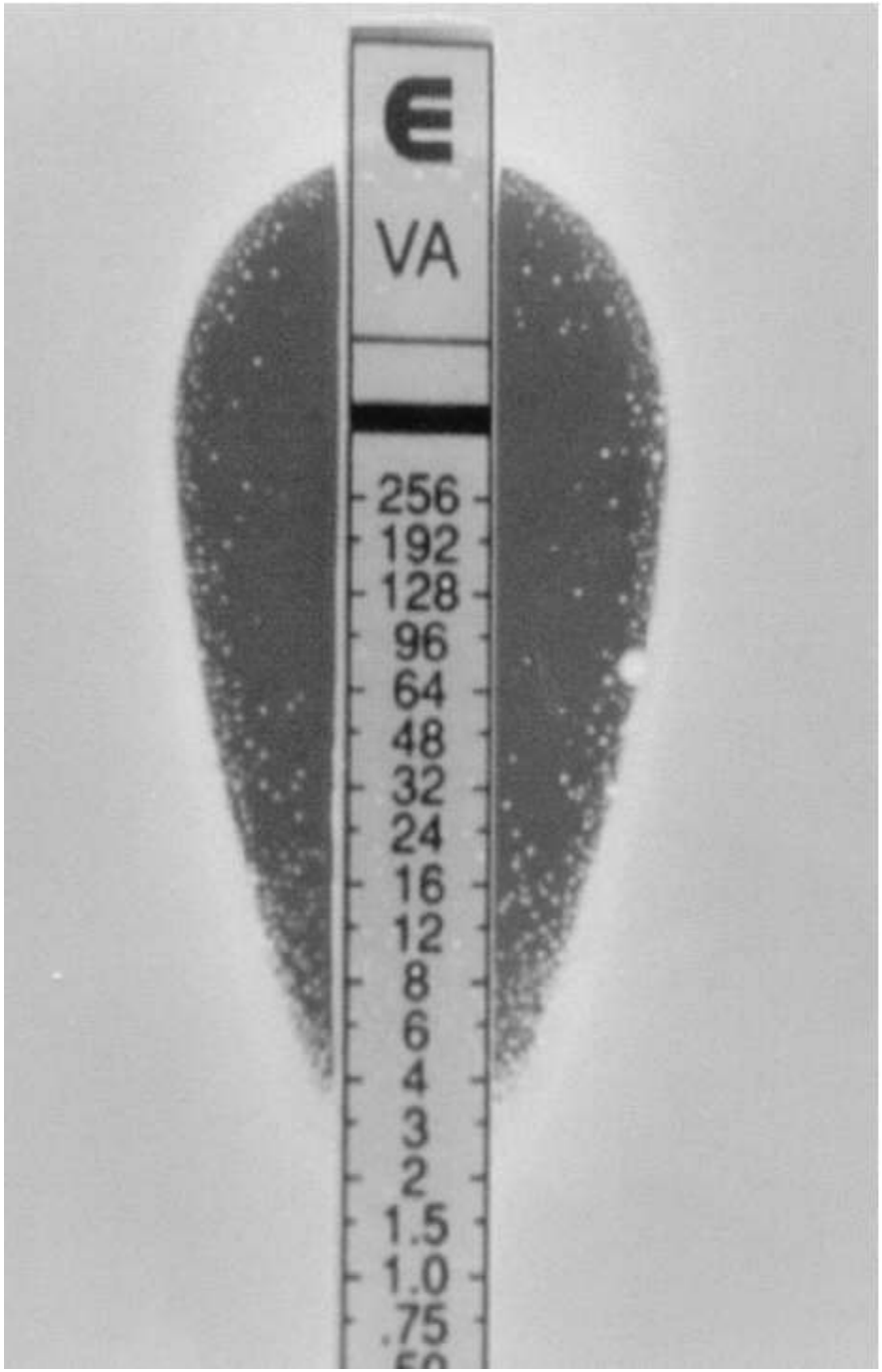
hVISA - Türkiye

- 1998-2002 Hacettepe - % 17.9 hVISA

  (MIC 0.5-4 mg/L) –

  Sancak B, JAC 2005; 56:519–23

- Güncel hVISA ?



The Prevalence of Vancomycin-Intermediate *Staphylococcus aureus* and Heterogeneous VISA Among Methicillin-Resistant Strains Isolated from Pediatric Population in a Turkish University Hospital

- ✓ 94 pediatrik MRSA
  - PAP-AUC and Etest makrometod.
- ✓ Tümü vankomisin ve daptomisine duyarlı
- ✓ 28 izolat (%29.8) vankomisin MİK 2 µg/ml (BMD).
  - %53 hVISA
- ✓ 20 (%21.3) hVISA (PAP-AUC).
  - %75 MİK 2 µg/ml.
- ✓ MİK kayması saptanmamış

Mirza Hasan Cenk, Sancak Banu, and Gür Deniz. Microbial Drug Resistance. October 2015, 21(5): 537-544.

RESEARCH ARTICLE | OPEN ACCESS

Vancomycin and daptomycin minimum inhibitory concentration distribution and occurrence of heteroresistance among methicillin-resistant *Staphylococcus aureus* blood isolates in Turkey

Banu Sancak ✉, Server Yagci, Deniz Gür, Zeynep Gülay, Dilara Ogunc, Güner Söyletir, Ata Nevzat Yalcin, Devrim Öztürk Dündar, Ayşe Willke Topçu, Filiz Aksit, Gaye Usluer, Cüneyt Özakin, Halis Akalin, Mutlu Hayran and Volkan Korten

BMC Infectious Diseases BMC series ¿ open, inclusive and trusted 2013 **13**:583 | **DOI:** 10.1186/1471-2334-13-583

- ✓ 175 MRSA kan izolatı, 2009-2010
  - 7 Üniversite hastanesi
- ✓ Vankomisin MİK >1 µg/ml
  - BMD ile %40.6
  - Etest ile %17.1
- ✓ hVISA %13.7

JOURNAL OF CLINICAL MICROBIOLOGY, May 2005, p. 2494–2496 Vol. 43, No. 5
0095-1137/05/$08.00+0 doi:10.1128/JCM.43.5.2494–2496.2005

Uns ical

- Stabil heteroresistans YOK
- %74 «unstable» heteroresistan
  - Artan vankomisin dozları ile

Div ;

Received 4 September 2004/Returned for modification 17 October 2004/Accepted 24 December 2004

We tested 109 unique, vancomycin-susceptible, methicillin-resistant *Staphylococcus aureus* (MRSA) strains for vancomycin heteroresistance by a selection method, i.e., step-wise exposure of large inoculums to increasing concentrations of vancomycin. Although no strains demonstrated stable heteroresistance, 81 strains (74%) demonstrated unstable heteroresistance. Unstable heteroresistance is common among clinical isolates of MRSA and may represent a cause of therapeutic failure.

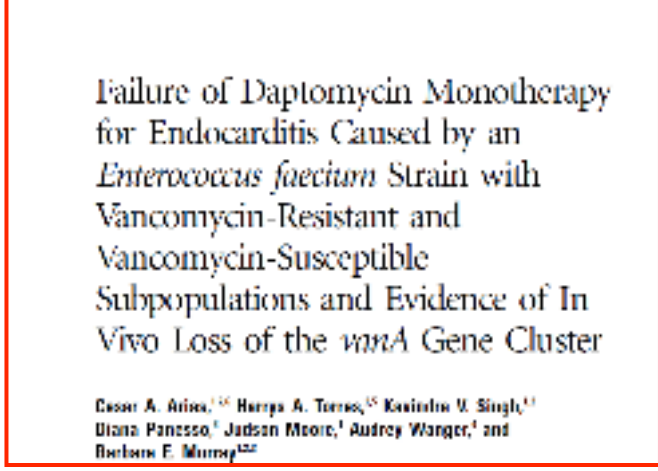
X. What is the management of persistent MRSA bacteremia and vancomycin treatment failures in adult patients?

- ✓ Daptomisin yüksek doz 10 mg/kg/gün
  - ○ Duyarlı ise kombine olarak;
    - Gentamisin, 8 saatte 1mg/kg
    - Rifampin , 600 mg/gün veya 2x300-450 mg
    - Linezolid 2x600 mg
    - TMP-SMZ 2x5mg/kg
    - Beta laktam

73. If reduced susceptibility to vancomycin and daptomycin are present, options may include the following: quinupristin-

- ✓ Vankomisin ve daptomisine azalmış duyarlılık varsa
  - ○ Duyarlı ise kombine olarak;
    - TMP-SMZ 2x 5mg/kg
    - Linezolid 2x600 mg
    - Televansin 1x10mg/kg

Olgu 2
60 y, K


Failure of Daptomycin Monotherapy for Endocarditis Caused by an *Enterococcus faecium* Strain with Vancomycin-Resistant and Vancomycin-Susceptible Subpopulations and Evidence of In Vivo Loss of the *vanA* Gene Cluster

Cesar A. Arias,[1,2] Hanya A. Torres,[2] Kavindra V. Singh,[1] Diana Panesso,[1] Judson Moore,[1] Audrey Wanger,[1] and Barbara E. Murray[1,2]

- ✓ DM
- ✓ 10 ay önce sağ aorta femoral by-pass,
  - sağ kasıkta MRSA + GBBHS enfeksiyonu
  - Sefepim 6 hafta + vankomisin 12 hafta
- ✓ 2 gündür devam eden nefes darlığı, göğüs ağrısı ve ateş
- ✓ FM'de 2/6 sistolik üfürüm
  - TTE'da ciddi mitral regürjitasyonla + mitral kapakta mobil vejetasyon
- ✓ Daptomisin (6 mg/kg /gün).
  - Kan kültürleri VR E- faecium
- ✓ Ardarda 3 negatif kan kültürü sonrası tedavi 6 haftaya tamamlanmak üzere taburcu

Daptomisin başlandıktan 5 hafta sonra…

- ✓ EKO'da persistan vejetasyon ve mitral kapak perforasyonu
  - Kan kültürü: Streptococcus spp + VS E. faecium
    - Daptomisin MİK 6 mcg/ml
  - Hasta kapak replasmanını reddeder
- ✓ Daptomisin kesilerek vankomisin (2 x 15 mg/kg + gentamisin (2 x 1 mg/kg) başlandı.
  - Kan kültürü 5. gün negatifleşir
- ✓ 5 hafta sonra rekürren endokardit
  - VR E. faecium; daptomisin MİK Etest ile 3 mg/L
    - gentamisin 2 x 1 mg/kg +
    - ampisilin 16 g/gün +
    - daptomisin 8 mg/kg /gün başlandı
  - 6 haftanın sonunda şifa
- ✓ 6 ay sonra dorunsuz

Strain	Date of isolation	Sample site	MIC, mg/L				Daptomycin MIC by Etest, mg/L
			Dapto[a]	Van[b]	Amp[c]	Gen[b]	
TX0133a	28 March 2006	Blood	4	512	32	8	6
TX0133b	9 May 2006	Blood	2	2	16	8	6
TX0133a.01	NA	Within the inhibition zone around the vancomycin Etest strip	2	1024	ND	8	6
TX0133a.04	NA	Outside the inhibition zone around the vancomycin Etest strip	4	1	ND	4	4
TX0133c	26 May 2006	Blood	2	512	64	4	3

AHA Scientific Statement

Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications

A Scientific Statement for Healthcare Professionals From the American Heart Association

Endorsed by the Infectious Diseases Society of America

Table 14. Vancomycin-Containing Regimens for Vancomycin- and Aminoglycoside-Susceptible Penicillin-Resistant *Enterococcus* Species for Native or Prosthetic Valve (or Other Prosthetic Material) IE in Patients Unable to Tolerate β-Lactam

Regimen	Dose* and Route	Duration, wk	Strength of Recommendation	Comments
Unable to tolerate β-lactams				
Vancomycin†	30 mg/kg per 24 h IV in 2 equally divided doses	6	*Class IIa; Level of Evidence B*	
Plus				
Gentamicin‡	3 mg/kg per 24 h IV or IM in 3 equally divided doses	6		
Penicillin resistance; intrinsic or β-lactamase producer				
Vancomycin plus aminoglycoside	30 mg/kg per 24 h IV in 2 equally divided doses	6	*Class IIb; Level of Evidence C*	For β-lactamase–producing strain, if able to tolerate a β-lactam antibiotic, ampicillin-sulbactam§ plus aminoglycoside therapy may be used.

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Recommendations

1. Patients with IE attributable to *Enterococcus* species resistant to penicillin, aminoglycosides, and vancomycin should be managed by specialists in infectious diseases, cardiology, cardiovascular surgery, clinical pharmacy, and, if necessary, pediatrics (*Class I; Level of Evidence C*).
2. If daptomycin therapy is selected, then doses of 10 to 12 $mg \cdot kg^{-1} \cdot 24\ h^{-1}$ may be considered (*Class IIb; Level of Evidence C*).
3. Combination therapy with daptomycin and ampicillin or ceftaroline may be considered, especially in patients with persistent bacteremia or enterococcal strains with high MICs (ie, 3 μg/mL) to daptomycin within the susceptible range (*Class IIb; Level of Evidence C*).

Table 15. Therapy for *Enterococcus* Species (

Regimen
Linezolid
Or
Daptomycin

IE indicates infective endoc
*Doses recommended are

g From

ents

ciated with potentially
ression, neuropathy,
ctions. Patients with IE
ould be treated by a care
in infectious diseases,
y, clinical pharmacy, and,
diac valve replacement
.

Daptomisin kombine kullanım

- Farklı etki ile kombinasyon mümkün
- Herhangi bir antagonistik etkiye rastlanmamış

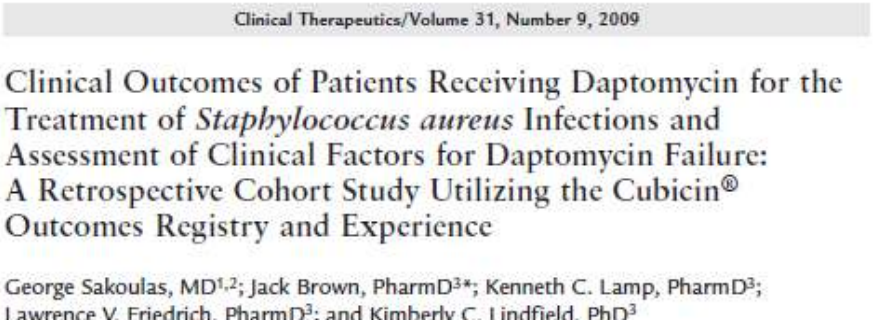
- Daptomisin bazı antibiyotiklerle kombine kullanımda sinerjistik bulunmuş:
  - Beta-laktamlar
  - MRSA ve VRE'ye karşı gentamisin
  - VRE ve Enterococcus faecium'a karşı rifampisin

1. Rand K.H. & Houck H. J. Antimicrob. Chemother. 2004;53:530-532 2. Snydman D.R., et al. J. Chemother. 2005;17:614-621 3. Pankey G., et al. Antimicrob. Agents Chemother. 2005;49:5166-5168.

Tedavi Başarısızlığı için Risk Faktörleri EU-CORE 2005-2007

%80 ikincil tedavi; %93 başarı

- ✓ Ciddi renal yetmezlik
- ✓ DM
- ✓ Eş zamanlı antibiyotik kullanımı
- ✓ Bakteriyemi
- ✓ Endokardit
- ✓ Önceki vankomisin kullanımı



Clinical Therapeutics/Volume 31, Number 9, 2009

Clinical Outcomes of Patients Receiving Daptomycin for the Treatment of *Staphylococcus aureus* Infections and Assessment of Clinical Factors for Daptomycin Failure: A Retrospective Cohort Study Utilizing the Cubicin® Outcomes Registry and Experience

George Sakoulas, MD[1,2]; Jack Brown, PharmD[3]*; Kenneth C. Lamp, PharmD[3]; Lawrence V. Friedrich, PharmD[3]; and Kimberly C. Lindfield, PhD[3]

Eur J Clin Microbiol Infect Dis (2011) 30:603–610
DOI 10.1007/s10096-010-1128-3

REVIEW

Emergence of daptomycin resistance following vancomycin-unresponsive *Staphylococcus aureus* bacteraemia in a daptomycin-naïve patient—a review of the literature

S. J. van Hal · D. L. Paterson · I. B. Gosbell

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Abstract A patient developed a daptomycin-resistant methicillin-resistant *Staphylococcus aureus* (MRSA) infection, despite being daptomycin-naïve, in the setting of persistent bacteraemia secondary to vertebral osteomyelitis. Modified population analysis profiling of sequential MRSA blood culture isolates revealed transition from a vancomycin-susceptible phenotype to a vancomycin-intermediate *S. aureus* (VISA) phenotype through a

these findings emphasise the importance of optimising management, including the consideration of early surgical intervention to avoid the emergence of daptomycin resistance, especially in high inoculum infections.

Daptomycin is a cyclic lipopeptide with proven efficacy for the treatment of *Staphylococcus aureus* skin and soft tissue

Endokardiyal Vejetasyon Simülasyonu ile FK/FD Modelleme

- ✓ 2 VRE. faecium; 1i Linezolid R
  - Dapto MİK= 4 ve 2mcg/ml
- ✓ 1 VRE. faecalis
  - Dapto MİK= 0.5 mcg/ml
- ✓ 6, 8, 10, 12mg/kg doz modeli
  - Tüm dozlarda bakterisidal
    - 6 ve 8 mg/kg ile etki devamlılık göztermiyor
    - 10 ve 12 mg /kg ile 96 saate kadar devam
  - E. faeciumda azalmış duyarlılık yok
  - E. faecalisde sadece 12mg/kg'da azalmış duyarlılık gösteren mutant yok

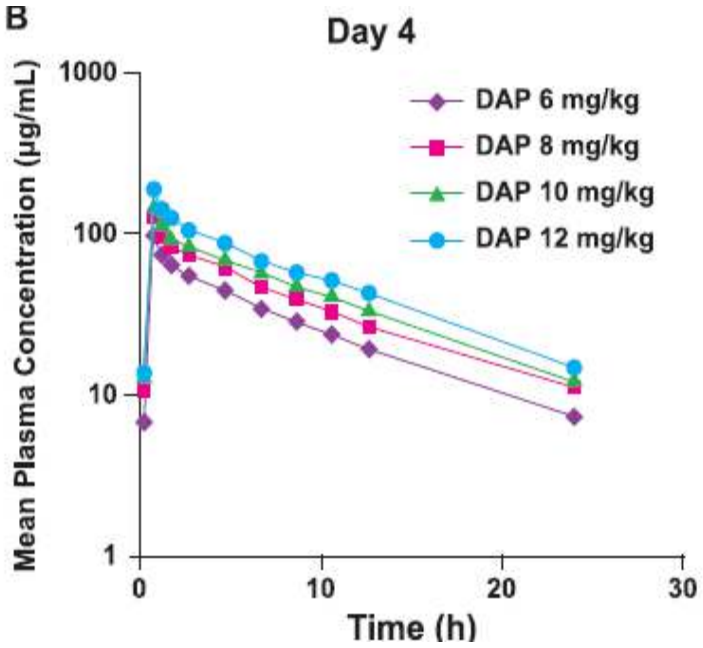
Evaluation of Standard- and High-Dose Daptomycin versus Linezolid against Vancomycin-Resistant *Enterococcus* Isolates in an *In Vitro* Pharmacokinetic/Pharmacodynamic Model with Simulated Endocardial Vegetations

Ashley D. Hall,[a] Molly E. Steed,[a] Cesar A. Arias,[a,b,c] Barbara E. Murray,[a,d,e] and Michael J. Rybak[a,b]

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Oct. 2006, p. 3245–3249 Vol. 50, No. 10
0066-4804/06/$08.00+0 doi:10.1128/AAC.00247-06

Pharmacokinetics and Tolerability of Daptomycin at Doses up to 12 Milligrams per Kilogram of Body Weight Once Daily in Healthy Volunteers

Mark Benvenuto,* David P. Benziger, Sara Yankelev, and Gloria Vigliani



daptomycin concentration. Daptomycin did not produce electrocardiographic abnormalities or electrophysiological evidence of muscle or nerve toxicity. Daptomycin was well tolerated in subjects dosed with up to 12 mg/kg intravenously for 14 days. Doses of daptomycin higher than 6 mg/kg once daily may be considered in further studies to evaluate the safety and efficacy of daptomycin in difficult-to-treat infections.

Özetle;

- ✓ Dirençli gram pozitif bakteri enfeksiyonlarının tedavisi için seçenekler eklenen yeni ajanlara rağmen azalmakta
- ✓ Doğru doz ile kullanım seçilen antibiyotik kadar önemli

Teşekkür ederim