İNFEKTİF ENDOKARDİT
VE DİĞER KARDİYOVASKÜLER İNFEKSİYONLARDA
TARTIŞMALI KONULAR: MULTİDİSİPLİNER YAKLAŞIMLAR

Ankara Üniversitesi İbn-i Sina Hastanesi
Hasan Ali Yücel Salonu, Ankara

İEÇG
KLİMİK DERNEĞİ İNFEKTİF ENDOKARDİT VE DİĞER
KARDİYOVASKÜLER İNFEKSİYONLAR ÇALIŞMA GRUBU

20-21 EYLÜL 2019

SOL TARAFLI İE'de ARDIŞIK ORAL TEDAVİ KANIT???

Yasemin TEZER TEKÇE

Sunum Planı

- İE antimikrobiyal tedavisinde genel özellikler
- Oral tedavi mümkün mü?
- Güncel kanıtlarda neler var? (Kronolojik sıra ile…)
- Hangi hastalara?
- Hangi ajanlar ile?
- Ardışık oral tedavinin **tek yer aldığı** uzlaşı raporu ne diyor?

NIH U.S. National Library of Medicine

ClinicalTrials.gov

Modify Search Start Over

93 Studies found for: **endocarditis**

List By

Show Filte

Showing: 1

Row

1

" id=

" aria-label="Save Study

checkbox"

onchange="updateCart('

Multidisciplinary

Consensus

Meeting

- 93 çalışmanın 40'ı tamamlanmış, sonlandırılmış ya da geri çekilmiş

- 12/53 çalışma cerrahi
- 12/53 görüntüleme
- 21/53 çalışma antimikrobiyal tedavi;

NIH U.S. National Library of Medicine

ClinicalTrials.gov

Modify Search Start Over

3 Studies found for: **oral and treatment and endocarditis**

List By

Show Filter

RSS

mns

Row

1

" id="

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checkbox"

onchange="updateCart('

Endocarditis

ns

ntibiotic

- Drug: Guideline treatment with par antibiotics

- 3/21 çalışma sol taraf İE ardışık oral tedavi ile ilgili

(1'i tamamlanmış, diğer ikisi devam etmekte)

İE Tedavinin Genel İlkeleri Ulusal Uzlaşı Raporu Ne Diyor?

- *25. İnfektif endokardit tedavisinin genel prensipleri nelerdir ve tedavi süreleri nasıl belirlenir?*

- İE'in antimikrobik tedavisinde genel ilkeler tedavinin sidal ajanlarla, **parenteral** yoldan ve uzun süreli kullanılmasıdır. Tedavi süresi, etkene, yabancı cisim varlığına ve yakınmaların süresine göre belirlenir. Bu süre doğal kapak endokarditlerinde genellikle 4-6 hafta, yapay kapak endokarditlerinde ise ≥6 haftadır.

İnfektif Endokarditin Tanısı, Tedavisi ve Önlenmesi: Ulusal Uzlaşı Raporu

Diagnosis, Treatment and Prevention of Infective Endocarditis: Turkish Consensus Report

Sol Kalp İnfektif Endokarditinde

- ESC ve AHA klavuzları doğrultusunda 6 haftalık tedavi
- Endokarditli hastalarda tanı ve tedavinin ilk aşamasında yakın takip ve yoğun bakım gerekebilmekte
- Patojen ve komplikasyonlara bağlı olarak hastane mortalitesi %15-45
- Hastaların yarısında cerrahi gerekmekte

Sol Kalp İnfektif Endokarditinde

- Komplikasyonların çoğu, mortalite de dahil olmak üzere hospitalizasyonun başlangıç kısmında

- Uzun süre hospitalizasyonun sebebi intravenöz (IV) tedavinin tamamlanması, kardiyak komplikasyonların ve komorbiditelerin takip ve tedavisi.

Uzun Süre Hospitalizasyonun Sakıncaları

- Uzun süreli yatıştan kaynaklanan artmış komplikasyon riski (HAI, katetere bağlı filebit, ekstravasazyon yaralanmaları, tromboz…)
- Diğer hastaların tedavisindeki negatif etki (hastalara bulaş, lojistik…)
- Sağlık bakımı ile ilişkili maliyeti artış

PLOS | MEDICINE

ESSAY

An Unsupported Preference for Intravenous Antibiotics

Ho Kwong Li[1], Ambrose Agweyu[2], Mike English[2,3], Philip Bejon[1,3,4]*

Hospitalizasyonu nasıl azaltırız?

- Parenteral tedavi süresini kısaltarak

  (2 haftalık tedavi) (Sol kalp İE☒)

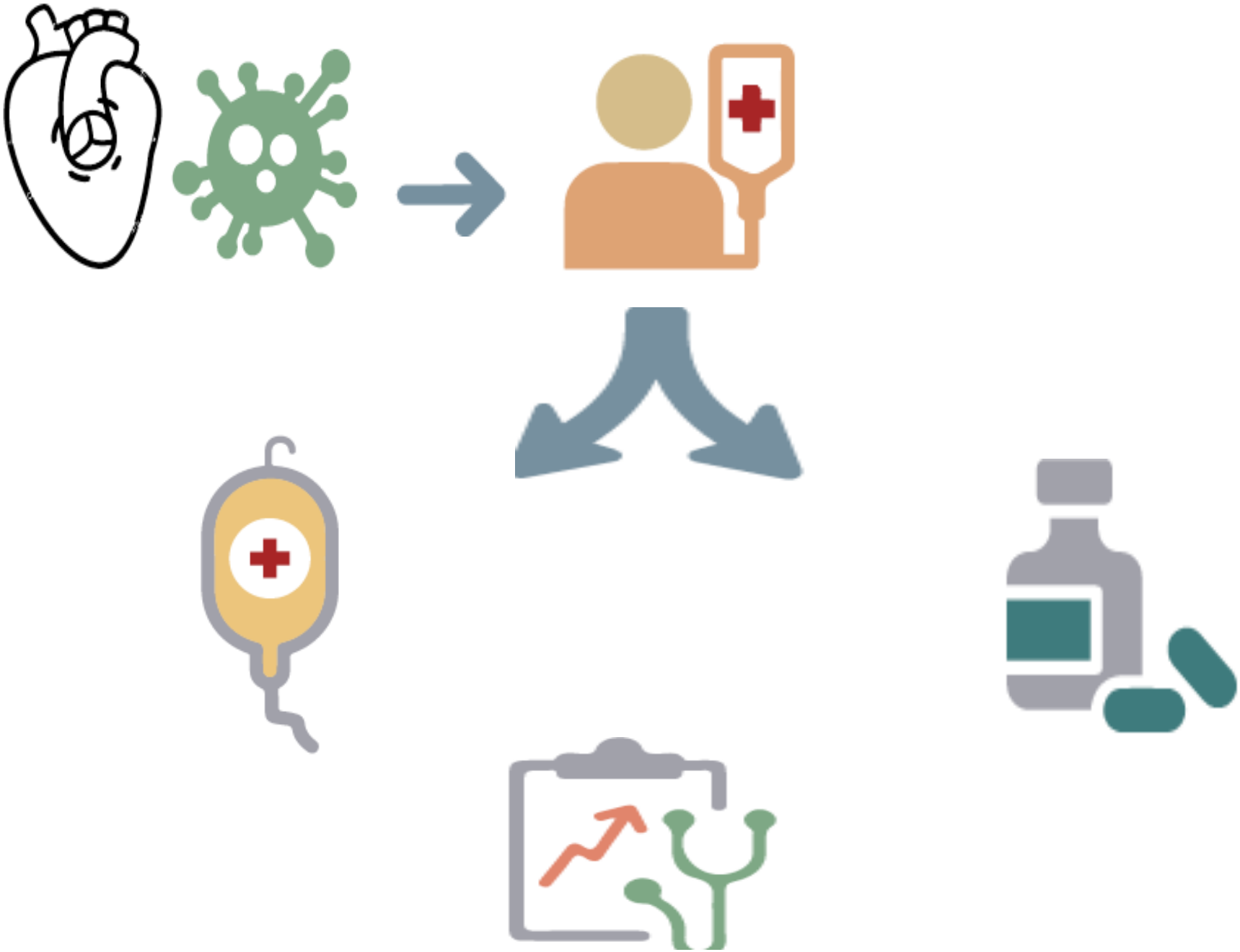
- APAT ile (sıklıkla ABD'de uygulanmakta)

ANCAK lojistik, hasta ve personel eğitimi, etkinlik ve advers olayların izlemindeki monitorizasyon sorunu, paramedikal ve sosyal destek ihtiyacı, ugulanabilirliğini KISITLAMAKTA!

Sol Kalp İnfektif Endokarditinde Oral Tedavi Alternatif Olabilir mi?

- Sadece oral tedavi ile?
- Güvenilirlik ve etkinliği için klinik kanıt çok kısıtlı ancak parenteral tedavi ile başlanıp klinik stabilizasyonu sonrası oral tedaviye geçiş yeniden gündemde…

Ardışık Oral Tedavi (PE→PO geçilerek)



ORIGINAL ARTICLE INFECTIOUS DISEASES

How do physicians cope with controversial topics in existing guidelines for the management of infective endocarditis? Results of an international survey

G. Béraud[1,2,3], C. Pulcini[4,5], J. R. Paño-Pardo[6], B. Hoen[7,8], B. Beovic[9] and D. Nathwani[10], on behalf of ESGAP

How long have you been practicing since graduation?	
Other	70 (11.2)
More than 10 years	433 (69.3)
Less than 10 years	192 (30.7)
Concerning the use of gentamicin in IE, is your practice based on:	
Guidelines (US 2005 and/or European 2009 and/or BSAC 2012)	455 (72.8)
Personal expertise	105 (10.4)
Department/facility protocol	65 (16.8)
Which dose of gentamicin do you use in a patient with endocarditis and normal renal function?	
3 mg/kg/day	394 (63.1)
4 mg/kg/day	77 (12.3)
5 mg/kg/day or more	154 (24.6)
Which regimen of gentamicin do you use in a patient with endocarditis due to *Staphylococcus* and with normal renal function?	
I usually don't use aminosides in staphylococcal IE	210 (33.6)
Once a day	204 (32.6)
Twice a day	73 (11.7)
Three times a day	138 (22.1)
Which regimen of gentamicin do you use in a patient with endocarditis due to *Streptococcus* and with normal renal function?	
I usually don't use aminosides in streptococcal IE	146 (23.3)
Once a day	248 (39.7)
Twice a day	75 (12.0)
Three times a day	156 (25.0)
Which regimen of gentamicin do you use in a patient with endocarditis due to *Enterococcus* and normal renal function?	
I usually don't use aminosides in enterococcal IE	62 (9.9)
Once a day	189 (30.2)
Twice a day	126 (20.2)
Three times a day	248 (39.7)
When do you monitor gentamicin peak concentrations in plasma?	
Never	283 (45.3)
At the beginning of treatment only	112 (17.9)
Regularly during treatment	230 (36.8)
When do you monitor gentamicin trough concentrations in plasma?	
Never	150 (24.0)
At the beginning of treatment only	42 (6.7)
Regularly during treatment	433 (69.3)
Do you sometimes switch to oral therapy for left-sided uncomplicated endocarditis when the clinical and microbiologic response to parenteral therapy has been good? (n = 621)	
Yes	195 (31.4)
No	427 (68.6)
For which clinical situations regarding left-sided endocarditis do you switch to oral therapy (considering the pathogen is susceptible to antibiotics with an excellent bioavailability)? (n = 188) (*several answers possible*)	
Streptococcal endocarditis	115 (61.2)
Enterococcal endocarditis	41 (21.8)
Staphylococcal endocarditis	66 (35.1)
Native valve endocarditis	116 (61.7)
Prosthetic valve endocarditis	24 (12.8)
Uncomplicated endocarditis	153 (81.4)
What is your first-line treatment for MRSA left-sided endocarditis on native valve (considering you don't have any MIC yet)? (n = 607) (*several answers possible*)	
Vancomycin	150 (24.7)
Vancomycin + gentamicin	309 (50.9)
Vancomycin + rifampicin	85 (14.0)
Daptomycin + rifampicin	40 (6.6)
Daptomycin + gentamicin	47 (7.7)
Linezolid	17 (2.8)

- Klavuzlarda yer almamasına rağmen ardışık oral tedavi katılımcıların %31.4'ü uygulamakta
- En az uygulayan %26 ile enfeksiyon hastalıkları uzmanları, en fazla uygulayanlar kardiyologlar ve klinik mikrobiyologlar

Clinical Microbiology and Infection, Volume 22 Number 2, February 2016

Open Forum Infectious Diseases IDSA Infectious Diseases Society of America hivma hiv medicine association

Article Navigation

ACCEPTED MANUSCRIPT

Practice patterns of infectious diseases physicians in transitioning from intravenous to oral therapy in patients with bacteremia

Duane R Hospenthal, C Dustin Waters, Susan E Beekmann, Philip M Polgreen

Open Forum Infectious Diseases, ofz386, https://doi.org/10.1093/ofid/ofz386
Published: 30 August 2019 **Article history**

- Katılımcıların %88'i PO ardışık tedaviyi GN bakteriyemilerde
- GP bakteriyemilerde ise %71'i
- %12'si hiçbir şekilde oral tedavi desteklememekte
- > %75'I Enterobactericea , pseudomonas ve *S. pneumoniae* oral tedavi güvenli
- **< %20 *S. aureus* ve endokarditlerde oral tedaviyi desteklemekte!!!**

ELSEVIER MASSON
Disponible en ligne sur ScienceDirect www.sciencedirect.com
Elsevier Masson France EM|consulte www.em-consulte.com
Médecine et maladies infectieuses
Médecine et maladies infectieuses 41 (2011) 602–607

Original article

udit of antibiotic therapy used in 66 cases of endocarditis☆

de la qualité de l'antibiothérapie chez 66 patients ayant une endocardite infectieuse

nchy [a], P. Dellamonica [a,b], P.M. Roger [a,b], E. Bernard [a], E. Cua [a], C. Pulcini [a,*,b]

2011

- 2007-2009 yılında Fransa'da tek merkezde retrospektif yapılan çalışmada 66 İE olgusununun **%29 (n:19)** parenteral başlanan tedaviden sonra ardışık oral tedaviye geçilmiş
- PE tedaviden 18 gün sonra PO
- Çoğu **komplike İE (n:15) ve/veya 12 sol kalp** İE;
- 8 MSSA, 4 MRSA
- 6'de monoterapi (3- FQ, 3- LZD)
- 6'da ikili tedavi (FQ+RİF, FQ+ klindamisin)
- 7 streptokokal İE'de ardışık tedavi uygulanmış (4'ü amoksisilin monoterapisi; amoksisilin+ RİF; Amoksisilin+ klindamisin)
- Ardışık tedavi uygulananlar, %79 gibi yüksek oranlarda komplike ve **%63'ü sol kalp İE olmasına** rağmen iyi sonuç!

Al-Omari *et al. BMC Infectious Diseases* 2014, **14**:140
http://www.biomedcentral.com/1471-2334/14/140

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Oral antibiotic therapy for the treatment of infective endocarditis: a systematic review

2014

- 6 gözlemsel, 2 klinik çalışma
- Raporlanmış yayınlarda oral tedavi ile kür oranları %77-100
- AB'lerin başarısı; m.o.'nın duyarlılığına, AB'in farmokokinetik özelliklerine (biyoyararlanım, dağılım ve vegetasyonda etkili konsantrasyonuna), uygun tedavi süresine bağlı bulunmuş

Gözlemsel çalışmaların ikisinde sol kalp İE

Table 1 Observational studies of oral antibiotic therapy for infective endocarditis

Reference	Cases	Design	Case definition	Microbiology	Assessment of antibiotic susceptibility	Therapy	Cure
Colli et al, Italy [9] 2007	12 NVIE and 2 PVIE requiring acute valve replacement(all left-sided)	Retrospective. Mean follow-up was 20.8 ± 7 months	By Duke criteria	MRSA (60%) *S. viridans* (30%) *Enterococcus sp.* (10%)	Yes	IV vancomycin for 5.3 ± 3.4 days followed by oral linezolid for 3 weeks	100%
Dworkin et al, USA [10]	13 IVDUs with NVIE (all right-sided with no systemic metastasis)	Prospective. 4-week follow-up	≥2 positive blood cultures AND any of the following: Vegetations on echocardiogram (definite – 3 cases) OR pulmonary infiltrates/ effusion or tricuspid insufficiency murmur (probable – 6 cases) OR no other identifiable source for the infection (possible – 1 case)	*S. aureus* (100%)	Yes	IV ciprofloxacin and oral rifampin for 1 week followed by oral ciprofloxacin and oral rifampin for 3 weeks	77%
Chetty et al, South Africa [11]	15 NVIE (right-sided vs. left-sided not specified, all cases were considered uncomplicated)	Prospective. 3-year follow-up	Characteristics clinical features AND any of the following: Positive blood cultures OR vegetations on echocardiogram	*Streptococcus sp.* (60%) Culture negative (40%)	Yes	High dose oral amoxycillin for 6 weeks (47% also received probenecid)	87%
Pinchas et al, Israel [12] 1983	11 NVIE (all left-sided, considered uncomplicated)	Prospective. Follow-up varied from 3 months to 12 years	Fever AND pre-existing valvular heart disease AND multiple positive blood cultures	*S. viridans* (100%)	Yes	High dose oral ampicillin for 6 weeks with probenecid for the first 4 weeks. IM streptomycin for the first 2 weeks	90%
Phillips et al, UK [13]	13 NVIE (right-sided vs. left-sided not specified) – all children	Retrospective. Follow-up varied from 1-15 years	Pre-existing valvular disease AND characteristic clinical features AND positive blood cultures	*S. viridans* (62%) *Staphylococcus sp.* (23%) Other streptococci or *Enterococcus sp.* (15%)	Yes	IV therapy for < 2 weeks (92% ≤3 days) followed by oral penicillin V, ampicillin, cloxacillin, flucloxacillin or erythromycin for 6-8 weeks	100%
Gray et al, UK [14]	13 NVIE (right-sided vs. left-sided not specified)	Retrospective. 3-month follow-up	Not specified	*S. viridans.* (62%) *E. faecalis* (1%) Culture negative (37%)	Yes	Oral ampicillin or propicillin (with or without probenecid) for 6 weeks	92%

Al-Omari *et al. BMC Infectious Diseases* 2014, **14**:140

Klinik çalışmaların birinde sol kalp İE

Table 2 Clinical trials of oral antibiotic therapy for infective endocarditis

Reference	Cases	Design	Case definition	Microbiology	Therapy	Results
Heldman et al, USA [18]	85 IVDUs with NVIE (all right-sided with no systemic metastases), 40 in the oral therapy arm and 45 in the IV therapy arm	Prospective, randomized, open label. 1-month follow-up	- ≥2 positive blood cultures AND any of the following: Valvular vegetations on echocardiogram (definite – 15 cases) OR evidence of pulmonary emboli on chest X-ray or tricuspid insufficiency murmur (probable – 26 cases) OR no other identifiable source for the infection (possible – 44 cases)	MRSA (5%) MSSA (89%) CoNS (6%)	Oral ciprofloxacin and rifampin for 4 weeks vs. IV oxacillin or vancomycin (IV gentamicin for the first 5 days) for 4 weeks	Cure rate: 90% (oral therapy) vs. 91% (IV therapy), $p = 0.9$ Treatment toxicity: 3% (oral therapy) vs. 62% (IV therapy), $p < 0.001$
Stamboulian et al, Argentine [19]	30 NVIE (all left-sided), 15 in each arm	Prospective, randomized, open label. 3 to 6-motnh follow-up	- ≥2 positive blood cultures AND any of the following: New or changing regurgitant murmur OR predisposing heart disease OR vascular phenomena OR valvular vegetation on echocardiogram	S. viridans (50%) S. bovis (50%)	IV or IM ceftriaxone for 2 weeks followed by high dose oral amoxicillin for 2 weeks vs. IV or IM ceftriaxone for 4 weeks	Cure rate: 100% in both arms. Treatment toxicity not reported

1991

Al-Omari et al. BMC Infectious Diseases 2014, 14:140

Clinical Microbiology and Infection 22 (2016) 607–612

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

Switch to oral antibiotics in the treatment of infective endocarditis is not associated with increased risk of mortality in non—severely ill patients☆

A. Mzabi [1,2], S. Kernéis [1,2,3], C. Richaud [1,2,3], I. Podglajen [1,2,3], M.-P. Fernandez-Gerlinger [1,2,3], J.-L. Mainardi [1,2,3,4,*]

2016

- 2000-2012 yılları arasında retrospektif kohort
  - 426 İE olgusu; %87 kesin, %13 olası
- En az 7 günlük PE tedavi sonrası PO tedavi ile devam edilen
- Günlük; hastanın genel durumu, kliniği, ateş kontrolü, CRP değerlerinde düşme, kan kültürlerinde üreme olmaması, lökositoz ve cre değerlerinin normalizasyonun takibi sonrası

Characteristic	Oral antibiotic switch (n = 214)	Exclusively intravenous route (n = 212)	p[a]
Definite endocarditis	179 (84)	190 (90)	0.09
Men	149 (70)	142 (67)	0.60
Age, years	65 (7–98)	64 (12–93)	0.62
Previous episode of IE	20 (9)	17 (8)	0.73
Congenital heart disease	20 (9)	15 (7)	0.48
Left heart endocarditis	161 (75)	174 (82)	0.10
Right heart endocarditis	15 (7)	12 (6)	0.69
Pacemaker endocarditis	33 (15)	19 (9)	0.05
Intracardiac device	5 (2)	7 (3)	0.57
Native valve endocarditis	125 (58)	137 (65)	0.20
Prosthetic valve endocarditis	51 (24)	49 (23)	0.91
Diabetes	15 (7)	30 (14)	0.02
Chronic renal failure	17 (8)	29 (14)	0.06
Cirrhosis	4 (2)	12 (6)	0.04
Immunosuppression	25 (12)	34 (16)	0.20
Temperature >38°C	183 (86)	183 (86)	0.89
Acute heart failure	60 (28)	94 (44)	$<10^{-4}$
Shock	9 (4)	36 (17)	$<10^{-4}$
Cerebral emboli	27 (13)	42 (20)	0.05
CRP, mg/L	81 (10–512)	88 (10–525)	0.06
Serum creatinine >100 μmol/L	76 (36)	110 (52)	$<10^{-4}$
Surgery	120 (56)	126 (59)	0.49
Streptococci	91 (43)	80 (38)	0.32
Coagulase-negative staphylococci	26 (12)	22 (10)	0.64
Enterococci	23 (11)	26 (12)	0.65
Staphylococcus aureus	28 (13)	53 (25)	0.002
Susceptibility			0.12
Methicillin-susceptible *S. aureus*	26 (12)	41 (19)	
Methicillin-resistant *S. aureus*	2 (1)	12 (6)	
No. of deaths/No. of patients followed up after diagnosis			
Day 10	0/214	18/212	
Day 30	1/188	25/200	
Day 90	4/144	20/170	

Hastaların 335'i (**%79) sol kalp İE**

Toplam hastaların 214'de (%50) de PO tedaviye geçiş

Sol kalp İE olgularının; 161 PO; 174 IV tedavi kollarında

A. Mzabi et al. / Clinical Microbiology and Infection 22 (2016) 607–612

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- **PO** grupta **daha az *S. aureus*** etkenli
- **PO grupta daha az** komorbidite, ve ciddi seyir (kalp yetmezliği, şok, serebral emboli gibi)
- Ortalama PO tedaviye geçiş süresi 21 gün

*streptokoklar için 14 gün, *S. aureus* için 28 gün, enterokoklar için 28 gün , diğer m.o.'lar için 21 gün sonra PO geçiş

- PO geçiş yapılanların %50'ne amoksisilin, diğerleri amoksisilin ve/veya rifampisin ile klindamisin ya da kinolon kombinasyonu

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- PO tedaviye geçiş yapılanlarla, PE tedavisi devam edilenlerin mortalite oranlarında anlamlı fark YOK
- Takiplerde PO grupta relaps ve reinfeksiyon oranlarında artmış risk YOK

2017

Clinical Microbiology and Infection 23 (2017) 124–125

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Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Letter to the Editor

Efficacy of the switch to oral antibiotics in the treatment of non-*Staphylococcus aureus* infective endocarditis in non-severely ill patients

- 13 yıllık retrospektif süreç, klavuz ve standart tedavi değişikliklerinin getirdiği, bilgi kaybının olabileceği olası yanlılık
- 2015 ESC klavuzunda zaten varolan MSSA bağlı sağ kalp İE PO
- PE tedavi kolunda daha fazla *S. aureus* İE (daha agresif ve mortalite oranı daha yüksek)
- PE tedavi kolunun daha ağır ve daha fazla komorbiditesinin olması seçimde yanlılığa sebep olabilir. O yüzden daha az ağır olan hastalar her iki kolda da karşılaştırılmalıydı.
- Tedavi süresi median 21 gün; ESC klavuzu 4 hafta önerisi gözönüne alındığında yeterli olabilir mi?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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.

2019

- Danimarka, çok merkezli, randomize, kör olmayan noninferiority çalışması
- Hipotez: Kliniği stabil sol taraf endokarditinde parenteral tedaviden oral tedaviye geçiş, etkinlik ve güvenilirlik açısından karşılaştırıldığında benzer

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

- 2011 ve 2017 yılları arasında
- 1954 sol kalp İE'li (Duke kriterleri+) vakadan 400'ü (%20) çalışmaya dahil edilmiş
- 199'u IV, 201'i PO gruba randomize
- Dışlanan hastalar; konfirme olmayan İE(522), onam alamamak (%16), diğer bakteriyel enfeksiyonlar (%9)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

***HANGİ HASTALAR?**

- >18y
- Modifiye Duke kriterlerine göre tanı almış sol nativ ya da protez kapak endokarditi
- Kan kültüründe streptokok, *Enterococcus faecalis, Staphylococcus aureus* ve KoNS üremeleri pozitif

Hangi Hastalar?

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*

- 4 bakteriden biri KK üremişse
- En az 10 gün , cerrahi geçirenlerde 7 gün PE tedavi almışsa
- Tedaviye klinik cevap;
- 2 gündür ateşsiz, CRP %25 azalma, 15000 altında lökosit
- TÖE da apse ve cerrahi gerektirecek patoloji olmaması
- PE tedavi ihtiyacı olmaması (azalmış GIS uptake ve BMI >40…)
- AB duyarlılık testinde biyoyararlanımı yüksek PO verilebilecek 2 tane AB varlığı

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

- Oral tedavi alan grup haftada 2-3 kere plk den takip
- Taburculuk sonrası ilk hafta,1,3 ve 6 ayda kontrol

- ORAL gruba, farmakokinetik özellikleri ve MİK değerleri gözetilerek, etki mekanizması ve metobolizması farklı (↓ GIS absorbsiyon ve hızlı metabolize), ayrı gruptan 2 AB

- PE gruba ESC ve Danimarka klavuzları doğrultusunda tedavi

- Her iki grupta da AB'lerin plazma seviyeleri yüksek basınçlı likit kromatografi ile takip

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. (%)		
Streptoco		
Enteroc		
Staphy		
Coagu		
Laborator		
Hemo		
Leuko		
C-reac		
Creati		
Preexistin dis		
Prosth		
Pacem		
Other		
Cardiac in no.		
Mitral-		
Aortic-		
Mitral- en		
Endoc		
Pacem		
Vegeta		
Moderate or severe valve regurgitation	19 (9.5)	23 (11.4)
Valve surgery during current disease course	75 (37.7)	77 (38.3)

- Her iki grup dağılımı benzer özellikler
- Hastaların %77 erkek
- Ortalama yaş 67
- 139 hasta (%35) en az bir komorbidite
- Randomizasyon sırasında her iki grp da kan
r (CRP
jen
kapak
esinde
ak
2/400
kapak
D

- Aort, mitral ya da aort+mitral kapak tutulumlararı
- Nativ/protez dağılımı
- Randomizasyon öncesi kapak cerrahisi uygulananlar

ARALARINDA ANLAMLI FARK YOK!

(Subgruplar homojen ve birbirleriyle etkileşimleri anlamlı DEĞİL!)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

- Endokardit tanısı ile randomizasyon arası medyan süre IV grp'ta 17 gün (13-23); PO grp'ta 17 gün (12-24)
- Rand. Sonrası tedavi süreleri IV grp'ta 19 gün (14-25), PO grp'ta 17 gün (14-25)
- Oral tedavi kolunda 160 hasta(%80) kısmen ya da tamamen tedavi ayaktan tamamlamış
- Rand. sonrası hastanede kalış süresi IV kolda 19 gün, PO grp'ta 3 gün

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

- 4 hasta oral tedavi grubundan PE'e geçiş (1 bulantı, 1 farklı mo ile bakteriyemi ve 2 kişisel tercih)
- Randomizasyon sonrası PE grupta 43 (%22) hasta, PO grupta 24 (%12) hasta farklı AB protokolleri ile takip

Hangi AB ‘ler?
Hangi Kombinasyonlar?

Penisilin ve metisilin Duyarlı *S aureus* ve CoNS’ler için;
(Pen S MSSA :27; MSCoNS:7)

1) Amoxicillin 1 g x 4 and fusidic acid 0.75 g x 2
2) Amoxicillin 1 g x 4 and rifampicin 0.6 g x 2
3) Linezolid 0.6 g x 2 and fusidic acid 0.75 g x 2
4) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2

Hangi AB ‘ler?
Hangi Kombinasyonlar?

MSSA ve CoNS’ler için,
(CoNS 15:S; MSSA 87:S)

1) Dicloxacillin 1 g x 4 and fusidic acid 0.75 g x 2

2) Dicloxacillin 1 g x 4 and rifampicin 0.6 g x 2

3) Linezolid 0.6 g x 2 and fucidic acid 0.75g x 2

4) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2

Hangi AB ‘ler?
Hangi Kombinasyonlar?

MRCoNS’ler için,
(8:R)

1) Linezolid 0.6 g x 2 and fusidic acid

2) Linezolid 0.6 g x 2 and rifampicin 0.6 g x2

Hangi AB ‘ler?
Hangi Kombinasyonlar?

Enterococcus faecalis için
(Amp MIC<4; 96:S)
(Amp MIC>4 1:R)

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

Hangi AB ‘ler?
Hangi Kombinasyonlar?

Penisilin MİK<1 mg/L Streptokoklar için
(194: S)

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

Hangi AB ‘ler?
Hangi Kombinasyonlar?

Penisilin MİK>1 mg/L Streptokoklar için
(2:R)

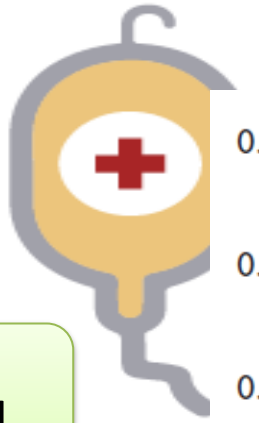
1) Linezolid 0,6 g x2 and rifampicin 0.6 g x 2

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

POET Çalışması

400 Hasta



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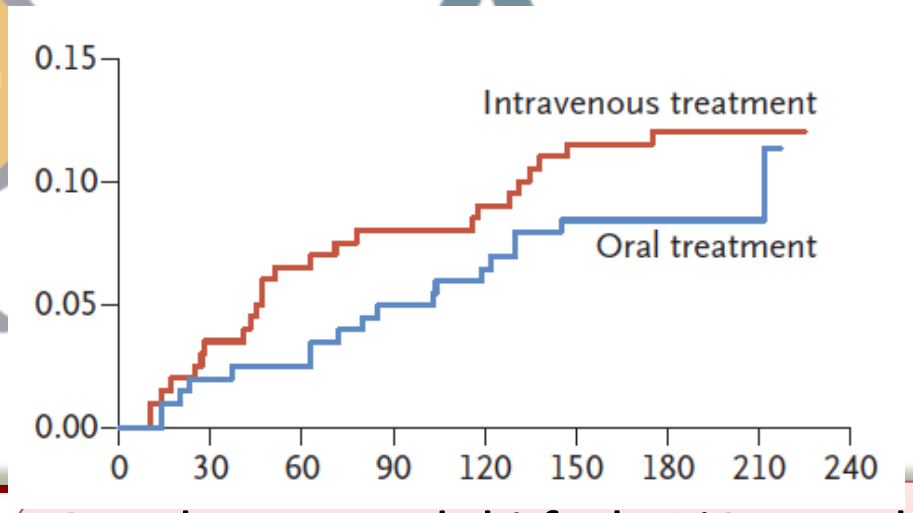


%9

PRİMEI

Tüm se

Planlan

Bakteri

Klinik o

Gruplar arasındaki fark %3.1 oral tedavi lehine non inf. kriterlerini karşılamakta

(Non inferiority margin %10)

POET Çalışma Sonuçları

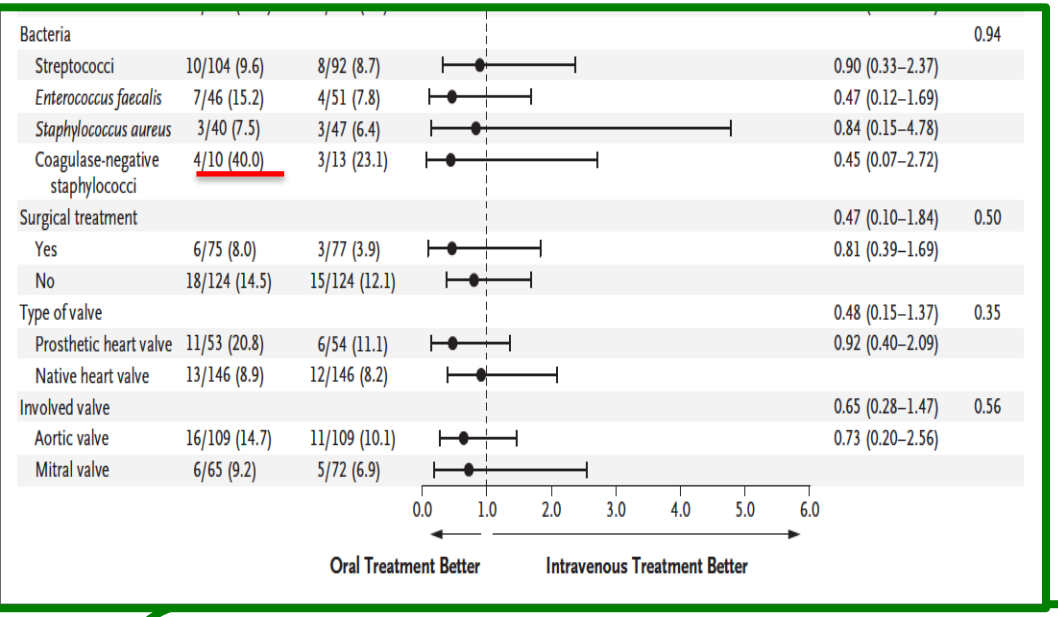
Table 2. Distribution of the Four Components of the Primary Composite Outcome.*

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.

- Embolik ataklar, planlanmamış kalp cerrahisi, bakteriyemi relapsı her iki grp'da da benzer.
- PO grp'da ölüm daha az!

POET çalışması
Primer Sonlanım noktasının bakteri türlerine göre analizi



Breakdown of bacterial species for each of the elements of the composite outcome

	All-cause mortality		Unplanned cardiac surgery		Embolic event		Relapse of positive blood culture	
	IV treatment n=13	Oral treatment n=7	IV treatment n=6	Oral treatment n=6	IV treatment n=3	Oral treatment n=3	IV treatment n=5	Oral treatment n=5
Streptococci	7 (54%)	3 (43%)	2 (33%)	4 (66%)	2 (67%)	2 (67%)	0	0
E faecalis	2 (15%)	1 (14%)	0	0	0	0	3 (60%)	3 (60%)
S aureus	2 (15%)	2 (28%)	3 (50%)	1 (17%)	0	0	2 (40%)	1 (20%)
CNS	2 (15%)	1 (14%)	1 (17%)	1 (17%)	1 (33%)	1 (33%)	0	1 (20%)

- Primer sonlanım noktası 4 bakteri tipinde de benzer.
- KNS'lerde primer sonlanım hızının fazla olması, tanısal gecikme ile yaşlı hastalar ve beraberindeki komorbiditelere bağlanmış.

ALTGRUPLARA GÖRE

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)		

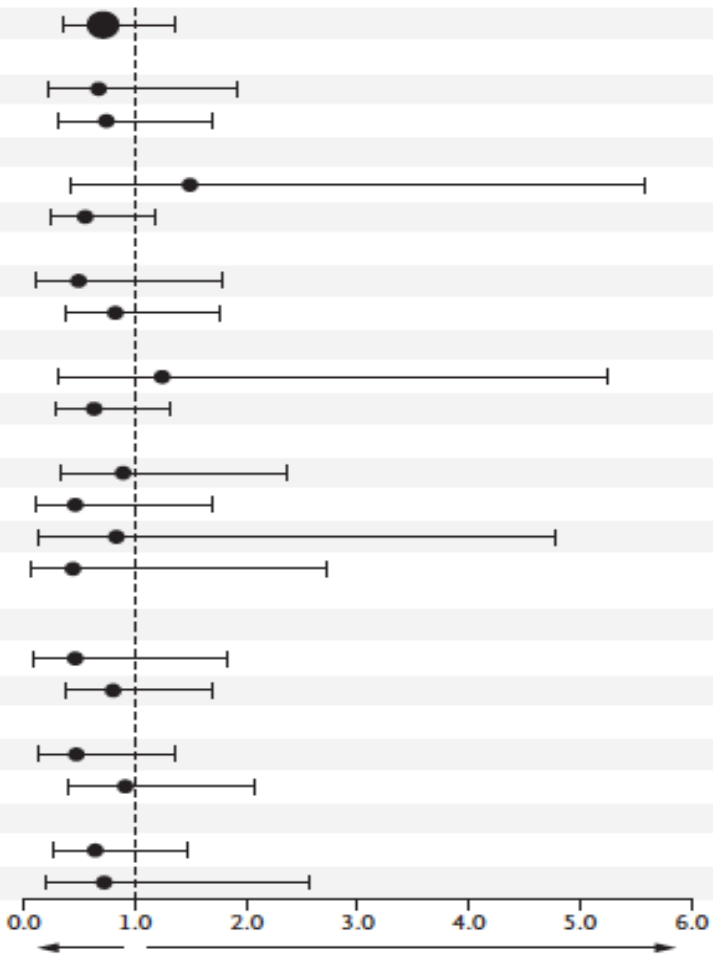


Figure 3. Rates of the Primary Outcome in Prespecified Subgroups.

POET Tartışma
Hangi antibiyotikler

- Subterapötik seviyelerde kalma riski (GIS uptake azalması, farmakokinetik varyasyonları elimine edebilmek için PO AB'ler farklı sınıflarda, farklı etki mekanizması ve farklı metabolize olanlardan seçilmiş.
- Yine de farmokokinetik ölçümler yapılmış ancak hiçbir hastada bunların sonucuna göre değişiklik yapılması gerekmemiş.
- O nedenle dikkatli seçilmiş AB'ler kullanılırsa farmokokinetik ölçüm yapmaya gerek olmayabilir??

Biyoyararlanımı ve doku geçişi iyi olan antibiyotikler

TABLE 1. **Penetration of Select Oral Antimicrobials to Tissue Sites**[7,44]

Antimicrobial	Bloodstream bioavailability	Lung	Liver	Urinary Tract	Prostate	Bone	GI	Skin	Bile	CSF	Synovial
Ciprofloxacin	70%	++	+++	+++	+++	+++	+++	+++	+++	+	+++
Levofloxacin	99%	+++	+++	+++	+++	+++	+++	+++	+++	+	+++
Moxifloxacin	90%	+++	+++	+++	+++	+++	+++	+++	+++	+	+++
Trimethoprim-Sulfamethoxazole	90%	++	++	+++	++	++	++	+++	++	+	++
Doxycycline	95%	++	++	++	++	++	++	++	++	+	++
Minocycline	95%	++	++	++	++	++	++	++	++	+	++
Linezolid	99%	+++	++	+++	++	++	++	+++	++	++	++
Metronidazole	90%	++	+++	++	++	++	++	++	++	++	++
Clindamycin	90%	++	++	++	++	++	++	++	++	+	++
Ampicillin	50%	+	++	++	+	++	++	++	++	++	+
Penicillin V	50%	++	++	++	+	++	++	++	++	++	+
Amoxicillin	85%	+	++	++	+	++	++	++	++	++	+
Cephalexin	60%	++	++	++	++	++	++	++	++	+	++

Journal of Hospital Medicine Published Online February 2018

Farmokokinetik ölçümlerdeki sorunlar

- PO grp'ta 7 hastada uygulanan 2 AB'den 1'i efektif plazma seviyesi sağlanamamış (Tepe değeri ve MİK üzerinde geçen süre ele alındığında)
- Rifampin alan 3 hasta, MXF alan 2 hasta, ve LZD alan 1 hasta
- Bu hastalarda primer sonlanım olmamış
- Farmokokinetik sonuçlar nedeniyle AB değişikliği yapılmamış.

POET Advers Etki

Randomizasyon sonrası toplam 22 (%6) hastada; p=0.66

12 (%6) IV kol

10 (%5) PO kol

En sık gözlenen advers etki allerji (%50), Kİ supresyonu (%27), GIS yakınmaları (%14)

Side effects	Intravenous treatment n=12	Oral treatment n=10
Gastro-intestinal symptoms, n (%)	0 (0)	3 (30.0)
Renal failure, n (%)	0 (0)	1 (10.0)
Hepatic failure, n (%)	0 (0)	1(10.0)
Bone marrow suppression, n (%)	2 (16.7)	4 (40.0)
Allergy, n (%)	10 (83.3)	1 (10.0)

POET Çalışmasının Kısıtlılıkları

- Sol kalp İE ele alınmış ancak beraberinde CIED ve sağ kalp İE olanlar çalışmadan çıkarılmamış
- Sadece belli bakteri türleri ile gelişen İE'ler çalışmaya dahil edilmiş. Kalan %25-30 diğer etken İE ya da kültür negatifler çalışmaya dahil edilmemiş.
- Batıda yaygın İE sebebi olan damardan ilaç bağımlılarında gelişen İE vakaları bu çalışmada sadece 5 hastada

POET Çalışmasının Kısıtlılıkları

- Dahil edilen hastaların sadece %22 ‘si *S. aureus* ,

hiç MRSA YOK!!!

SORUN MU????

Archives of Cardiovascular Disease (2016) 109, 542—549

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CLINICAL RESEARCH

Comparison of prognoses of *Staphylococcus aureus* left-sided prosthetic endocarditis and prosthetic endocarditis caused by other pathoge

- *S. aur*
  multi
- 4 yıll

Tablo 12. İnfektif Endokarditli Hastalarda Kötü Prognoz Belirteçleri

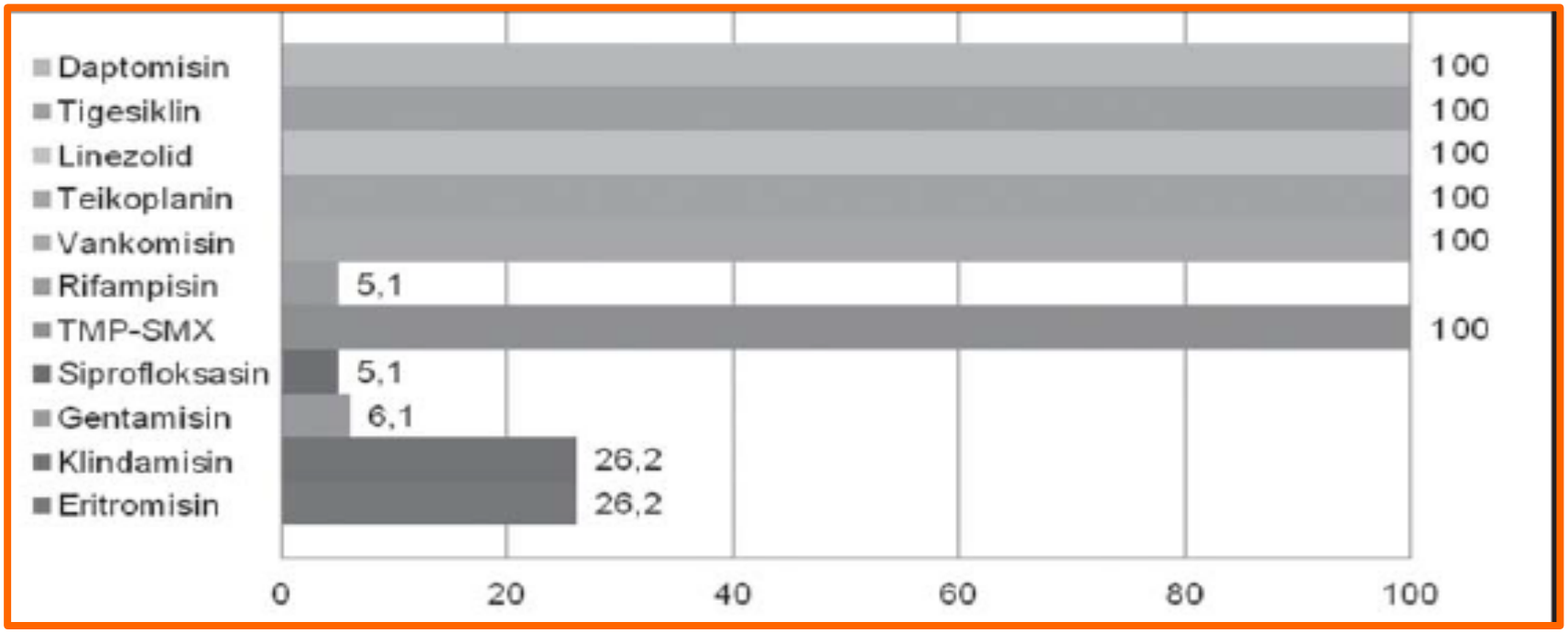
Etken Mikroorganizma
Staphylococcus aureus
HACEK dışı Gram-negatif çomaklar
Mantarlar

Tedavi seçenekleri kısıtlı!!!!

uksek.
, sepsis
ve geç cerrahi etkili.

POET Çalışmasının Kısıtlılıkları AB Direnci Yüksek Yerlerde??

- Yazarlar AB direnci yüksek olan yerlerde de ardışık oral tedavinin uygulanabileceğini düşünmekte.
- Çünkü AB duyarlılığına göre AB seçiminin yapıldığını öne sürmekteler.
- Ancak yüksek direnç görülen bölgelerde AB seçenekleri çok kısıtlı olabilir



2004-20111 yılları HÜTF

Kan kültüründe üreyen 147 MRSA suşu

Rif duyarlılığı %5

Cip duyarlılığı %5

Klindamisin duyarlılığı %26

Mikrobiyol Bul 2014; 48(4): 523-537

Table 3 Prevalence of resistance rates of 397 MRSA isolates

Antibiotics	Number of isolate (%)		
	Resistance rates	Intermediate resistance rates	Susceptibility rates
Erythromycin	225 (56.7)	64 (16.1)	108 (27.2)
Lincomycin	168 (42.3)	66 (16.6)	163 (41.1)
Tetracyclin	350 (88.2)	0	47 (11.8)
Ciprofloxacin	366 (92.2)	4 (1)	27 (6,8)
Kanamycin	363(91.4)	1 (0.3)	33 (8.3)
Gentamycin	358 (90.2)	5 (1.3)	34 (8.5)
Fusidic Acid	32 (8.1)	0	365 (91.9)
Linezolid	0	0	397 (100)
Vancomycin	0	0	397 (100)

12 merkezin katılımıyla

397 MRSA

Fusidik asit duyarlılığı %91.8

Cip. Duyarlılığı %6.8

Yıldız *et al. Annals of Clinical Microbiology and Antimicrobials* 2014, **13**:44

Türkiye MRSA Direnç Profili

Journal of Global Antimicrobial Resistance 6 (2016) 44–49

Contents lists available at ScienceDirect

Journal of Global Antimicrobial Resistance

journal homepage: www.elsevier.com/locate/jgar

Epidemiological and molecular characteristics of meticillin-resistant *Staphylococcus aureus* in Turkey: A multicentre study

Devrim Dündar [a,*], Ayse Willke [a], Murat Sayan [a,b], Meliha Meric Koc [a], Ozay Arıkan Akan [c], Bulent Sumerkan [d], Nese Saltoglu [e], Akgun Yaman [f], Celal Ayaz [g], Iftihar Koksal [h]

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ABSTRACT

The aim of this study was to investigate the epidemiological and molecular features of clinical meticillin-resistant *Staphylococcus aureus* (MRSA) isolates in Turkey. MRSA isolates were collected from six regions of Turkey. The *mecA* and *nuc* genes were detected by PCR. Antimicrobial susceptibilities were determined by the disk diffusion method. Staphylococcal cassette chromosome *mec* (SCC*mec*) and staphylococcal protein A (*spa*) typing were performed by the sequencing method for 270 randomly selected MRSA isolates. The US Centers for Disease Control and Prevention (CDC) definition was used for epidemiological diagnosis of community-associated MRSA (CA-MRSA). Resistance rates of MRSA to ciprofloxacin, gentamicin, clindamycin, erythromycin, rifampicin, trimethoprim/sulfamethoxazole and tetracycline were 93.4%, 81.2%, 38.5%, 57.8%, 93.9%, 1.1% and 93.1%, respectively. The most frequent SCC*mec* type was SCC*mec* III (91.1%). SCC*mec* type IV was found in 5.2% of the isolates. The most frequent *spa* type was t030 (81.1%). Five isolates were CA-MRSA if only the epidemiological definition was used (5/725; 0.7%). Two isolates were defined as CA-MRSA both by epidemiological features and SCC*mec* typing (2/270; 0.7%). Of 14 SCC*mec* type IV isolates, 12 were not defined as CA-MRSA by epidemiological features. In conclusion, this is the most comprehensive multicentre study in Turkey investigating MRSA using both epidemiological and genotypic features. The CA-MRSA rate is low in Turkey. Combined use of epidemiological and genotypic methods is the most accurate approach for the diagnosis of CA-MRSA.
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Toplum kökenli MRSA az

- Cipro R oranı;%93.4
- Klindamisin R; %38.5
- Eritromisin R; %57.8
- Rifampisin R:%93.9
- SXT R; %1.1
- Tetrasiklin R;%93.1

NEW MICROBIOLOGICA, 34, 187-193, 2011

Erythromycin and penicillin resistance mechanisms among viridans group streptococci isolated from blood cultures of adult patients with underlying diseases

Alper Ergin[1], Özgen Köseoğlu Eser[2], Gülşen Hasçelik[2]
[1]Hacettepe University, School of Health Services, Medical Laboratory Programme, Ankara, Turkey;
[2]Hacettepe University, Faculty of Medicine, Department of Medical Microbiology, Ankara, Turkey

Kan kültüründe üreyen 50 *Streptococcus viridans*

Çoğu altta yatan maligniteli hasta , 1 tane İE

- *%22 Pen S, %48 Pen I, %30 Pen R*
- *%40 Tetrasiklin R*
- *%30 Klindamisin R*
- *%20 sefotaksim R*
- *Van, Kloramfenikol, LVX, LZD %100 S*

Le Infezioni in Medicina, n. 3, 190-193, 2016

ORIGINAL ARTICLE

Antimicrobial susceptibility against penicillin, ampicillin and vancomycin of viridans group Streptococcus in oral microbiota of patients at risk of infective endocarditis

Serap Süzük[1], Banu Kaşkatepe[2], Mustafa Çetin[3]

İE riski olan 49 hasta

Group name	*No. (%)*	*Penicillin*		*Ampicillin*	
		Not susceptible No. (%)*	*Susceptible No. (%)*	*Not susceptible* No. (%)*	*Susceptible No. (%)*
S. mitis Group	16 (32.65%)	8 (50.00)	8 (50.00)	4 (25.00)	12 (75.00)
S. anginosus Group	16 (32.65%)	9 (54.25)	7 (43.75)	11 (68.75)	5 (31,25)
S. sanguinis Group	8 (16.33%)	6 (75.00)	2 (25.00)	6 (75.00)	2 (25.00)
S. mutans Group	6 (12.24%)	4 (66.67)	2 (33.33)	3 (50.00)	3 (50.00)
S. salivarius Group	3 (6.12%)	3 (100.00)	0 (0)	3 (100.00)	0 (0)

Le Infezioni in Medicina, n. 3, 190-193, 2016

(POET)Tablodaki Yanlış/lar?? Zorluklar?

Table S10

Antibiotic regimens in the POET trial.

	Oral regimens	
Staphylococcus aureus	Dicloxacillin and rifampicin	
	Amoxicillin and rifampicin	
	Moxifloxacin and rifampicin	
	Amoxicillin and fusidic acid	
	Dicloxacillin and fusidic acid	
	Fusidic acid and linezolid	
	Rifampicin and linezolid	
	Penicillin and rifampicin	
	Amoxicillin and clindamycin	
	Ampicillin and rifampicin	
	Moxifloxacin and fusidic acid	
	Moxifloxacin and linezolid	
	Linezolid and clindamycin	
Enterococcus faecalis	Amoxicillin and moxifloxacin	
	Amoxicillin and linezolid	15 (
	Amoxicillin and rifampicin	
	Moxifloxacin and linezolid	
	Amoxicillin and ciprofloxacin	
	Amoxicillin	
Streptococci	Amoxicillin and rifampicin	
	Amoxicillin and moxifloxacin	
	Rifampicin and linezolid	
	Moxifloxacin and linezolid	
	Amoxicillin and linezolid	
	Penicillin	
	Ampicillin and moxifloxacin	
	Ampicillin and rifampicin	
	Dicloxacillin and moxifloxacin	
	Moxifloxacin and clindamycin	
	Moxifloxacin and vancomycin	
Coagulase negative staphylococci	Fusidic acid and linezolid	
	Rifampicin and linezolid	4 (
	Amoxicillin and linezolid	1 (8)
	Dicloxacillin and rifampicin	1(8)
	Moxifloxacin and linezolid	1(8)
	Rifampicin and Fusidic acid	1(8

Dikloksasilin? Eksternal validite??

Beraberinde *C. difficile??*

Günde 12 tablet almak ve takip etmek KOLAY DEĞİL!

Tablodaki Yanlış/lar??

Zorlukla

İlaç etkileşimleri ve advers olaylar (Rifampin,LZD /serotonin!!!, Kinolonlar ve QT uzaması,FDA uyarısı..

Table S10

Antibiotic regimens in the POET trial.

	Oral regimen	
Staphylococcus aureus	Dicloxacillin a	
	Amoxicillin an	
	Moxifloxacin a	
	Amoxicillin and	
	Dicloxacillin an	
	Fusidic acid an	
	Rifampicin and	
	Penicillin and rif	
	Amoxicillin and cli	
	Ampicillin and rifampici	
	Moxifloxacin and fusidic a	
	Moxifloxacin and linezolid	
	Linezolid and clindamycin	
Enterococcus faecalis	Amoxicillin and moxifloxacin	24 (47)
	Amoxicillin and linezolid	13 (25)
	Amoxicillin and rifampicin	6 (12)
Streptoco		
Coagulase negative staphylococci	Fusidic acid and linezolid	5 (38)
	Rifampicin and linezolid	4 (31)
	Amoxicillin and linezolid	1 (8)
	Dicloxacillin and rifampicin	1(8)
	Moxifloxacin and linezolid	1(8)
	Rifampicin and Fusidic acid	1(8)

YAZARLARIN YANITLARI:

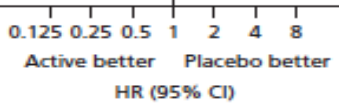
KC hastalığı olanlarda fusidik asit ve rifampin tercih edilmemiş, Platelet ve lökosit sayısı düşük olanlarda LZD tercih edilmemiş

Abstract

Adjunctive rifampicin to reduce early mortality from *Staphylococcus aureus* bacteraemia: the ARREST RCT

Guy E Thwaites,[1,2]* Matthew Scarborough,[1] Alexander Szubert,[3]

	Placebo	Active	(95% CI)	*p*-value
Initial active antibiotic (class level)				
(1) MSSA: penicillin(s)/cephalosporin(s)/carbapenem(s)	54/266 (20.3%)	38/245 (15.5%)	0.79 (0.52 to 1.20)	0.35
(2) MSSA: glycopeptide ± (1)	6/52 (11.5%)	8/58 (13.8%)	1.18 (0.41 to 3.41)	
(3) MSSA: (1) and other	5/33 (15.2%)	6/32 (18.8%)	1.40 (0.43 to 4.58)	
(4) MSSA: other	3/16 (18.8%)	1/9 (11.1%)	0.69 (0.07 to 6.67)	
(5) MRSA	3/21 (14.3%)	9/26 (34.6%)	2.74 (0.74 to 10.15)	
Initial active antibiotic (antibiotic level)				
MSSA: flucloxacillin only	38/191 (19.9%)	16/176 (9.1%)	0.45 (0.25 to 0.81)	0.01
MSSA: flucloxacillin and vancomycin/other	12/71 (16.9%)	17/67 (25.4%)	1.66 (0.79 to 3.47)	
MSSA: other penicillin(s)/cephalosporin(s)/carbapenem(s)	7/30 (23.3%)	10/31 (32.3%)	1.59 (0.60 to 4.18)	
MSSA: vancomycin ± other	7/56 (12.5%)	9/54 (16.7%)	1.36 (0.51 to 3.65)	
MSSA: other	4/19 (21.1%)	1/16 (6.3%)	0.32 (0.04 to 2.89)	
MRSA	3/21 (14.3%)	9/26 (34.6%)	2.74 (0.74 to 10.15)	
Intravenous catheter/implanted vascular device associated?				
No	61/298 (20.5%)	51/289 (17.6%)	0.90 (0.62 to 1.30)	0.34
Yes	9/88 (10.2%)	11/80 (13.8%)	1.44 (0.60 to 3.48)	
Endocarditis				
No endocarditis	66/370 (17.8%)	60/347 (17.3%)	1.02 (0.72 to 1.45)	0.13
Endocarditis	5/18 (27.8%)	2/22 (9.1%)	0.30 (0.06 to 1.54)	
Foci of infection known				
Foci of infection not known	14/66 (21.2%)	17/67 (25.4%)	1.31 (0.65 to 2.66)	0.30
Foci of infection known	57/322 (17.7%)	45/302 (14.9%)	0.87 (0.59 to 1.29)	
Age at last birthday (years)				
18–54	11/126 (8.7%)	8/125 (6.4%)	0.76 (0.31 to 1.89)	0.57
> 54–72	17/126 (13.5%)	13/122 (10.7%)	0.81 (0.39 to 1.67)	
> 72	43/136 (31.6%)	41/123 (33.3%)	1.15 (0.75 to 1.77)	



Drug-Drug Interaction Between Rifampin And Linezolid: Is It A Big Deal?

Is the drug-drug interaction between rifampin and linezolid worth worrying about? In this article two infectious diseases pharmacists discuss existing data on the topic.

Authored By: Ryan Stevens, Pharm.D., BCPS, BCIDP **and** Christina Rivera, Pharm.D., BCPS, AAHIV-M

LZD/Rif Etkileşimi İle İlgili Olgu raporları

Reference	Title	Design	Case Descriptions	Case Outcomes	Author Conclusion
Pharmacology. 2016; 98: 51–55.	Decreased linezolid serum concentration in three critically Ill patients: Clinical case studies of a potential drug interaction between linezolid and rifampicin	Case series [3 cases]	**Case 1:** 67 y/o with IVC ventriculitis on CVVHD treated with rifampin 600 mg daily + linezolid IV 600 mg q12h **Case 2:** 72 y/o treated for shoulder empyema with rifampin 600 mg q12h + linezolid 600 mg q12h **Case 3:** 77 y/o with *S. epidermidis* PJI treated linezolid 600 mg q8 + rifampin 450 mg q12h	**Case 1**: Linezolid C_{min} undetectable while on rifampin, then increased to 2 µg/mL after rifampin stopped **Case 2:** Linezolid C_{min} ranged at 0.6-0.8 µg/mL despite linezolid dose increases to 1800 mg/24h then 2700 mg/24h **Case 3:** linezolid C_{min} 0.5 - 1.9 µg/dL	When linezolid is used with rifampin, linezolid levels should be monitored.
Journal of Infection and Chemotherapy. 2016; 22(5): 331-4.	Successful treatment of methicillin-resistant *Staphylococcus aureus*	Case report	79 y/o F with MRSA PJI treated with linezolid 600 mg q12h + rifampin 450 mg q12h and vancomycin impregnated spacer	Maintained C_{min} within range of 3.7 - 7.2 µg/mL. Reported clinical improvement of	Monitor linezolid $C_{min, ss}$ at day 3 and periodically in patients on linezolid and rifampin.
Scandinavian Journal of Infectious Diseases. 2012; 44: 548–550.					Clinical failures were attributed to linezolid - rifampin. Monitor linezolid concentrations when using this combination.
*Pharmacotherapy.*2007; 27(3): 476–479.	levels in a critically Ill patient receiving concomitant linezolid and rifampin		MRSA neck abscess and bacteremia on linezolid 600 mg IV q12 and rifampin 300 mg IV q8	with rifampin. Linezolid was increased to 600 mg q8, resulting in a C_{min}=2 µg/dL with, C_{max} = 7 µg/dL. After rifampin was discontinued, linezolid further increased to C_{min}=5 µg/dL and C_{max}=12.5 µg/dL	Linezolid and rifampin lead to decreased serum linezolid levels in a critically ill patient.

Linezolid +rifampisin kombinasyonunda tedavi başarısızlığı!!
Kombinasyon tedavilerinde serum seviyeleri takip edilmeli!

LZD /Rif etkileşimi ile ilgili farmokokinetik çalışmalar

Reference	Title	Design	Interventions	Outcomes	Author Conclusion
Journal of Antimicrobial Chemotherapy. 51 (4), 857-864.	In vitro activity of linezolid alone and in combination with gentamicin, vancomycin or rifampicin against methicillin-resistant *Staphylococcus aureus* by time–kill curve methods	In vitro time-kill curves	Time–kill curves were performed over 24 h at *Staphylococcus aureus* inoculum of 5×10^6– 1×10^7 cfu/mL. Linezolid was studied at concentrations of 1×, 4×, 8× MIC, with partner drugs at 8 ×MIC.	Linezolid added to gentamicin and vancomycin decreased antibacterial activity. Linezolid with rifampicin showed synergism for rifampin susceptible strains and also inhibition of rifampicin-resistant variants	Linezolid plus rifampicin was the most active combination tested against *Staphylococcus aureus* strains in these time–kill experiments.
Clinical Pharmacology & Therapeutics. 2005; 77.5: 451-453.	Linezolid and rifampin: Drug interaction contrary to expectations?	PK analysis [8 healthy subjects]	D1: Single dose 600 mg linezolid IV given; D2 Single doses 600 mg linezolid IV + 600 mg rifampin IV given	D2: Linezolid level decreased to 90% at 6h, 80% at 9h, then to 65% at 12h	Suggests a Pg-P mediated drug interaction between linezolid and rifampin.
Journal of Clinical Pharmacology, 2011; 51: 229-236.					Linezolid with rifampin was safe and well tolerated. Linezolid exposure was decreased when given with rifampin.

Zaman- ölüm deneylerinde *S. aureus*'a karşı en etkili kombinasyon

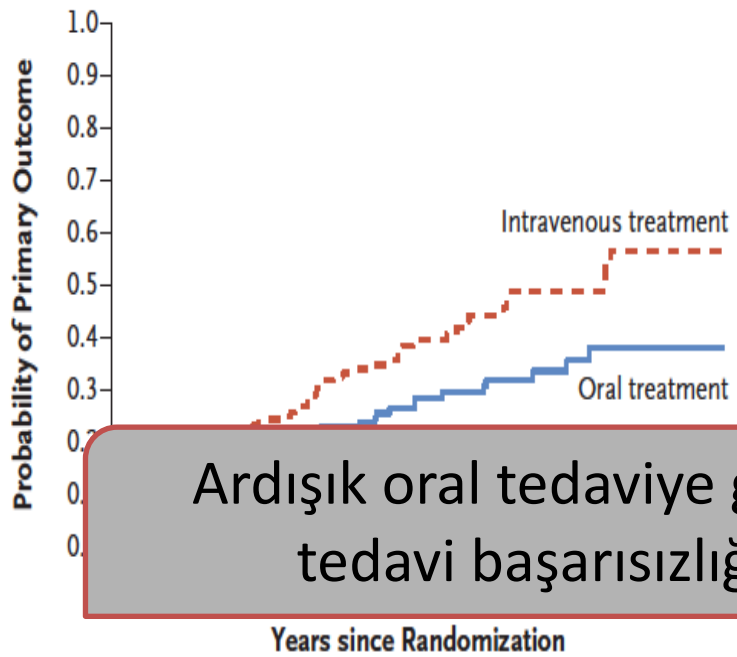
Rifampisin ile kullanıldığında, Linezolid seviyeleri düşük!

2019

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Long-Term Outcomes of Partial Oral Treatment of Endocarditis



No. at Risk

Intravenous treatment	199	168	126	88	56	33	20	4
Oral treatment	201	175	136	99	66	43	25	6

Figure 1. Cumulative Incidence Plot of the Primary Composite Outcome.

Ardışık oral tedaviye geçişte geç dönemde tedavi başarısızlığına rastlanmadı!

- Median izlem süresi 3.5 yıl
- Primer birleşik sonlanım noktası IV kolda %38.2, PO kolda %26.4
- Gruplar arasında cerrahi, elaps yok. ölüm IV kolda %27.8, PO kolda%16.4

2019

[m5G;July 2, 2019;10:15]
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High-dose trimethoprim-sulfamethoxazole and clindamycin for *Staphylococcus aureus* endocarditis

Hervé Tissot-Dupont[a], Frédérique Gouriet[a], Leopold Oliver[c], Matthieu Jamme[d], Jean-Paul Casalta[a], Marie-Thérèse Jimeno[e], Florent Arregle[b], Cécile Lavoute[b], Sandrine Hubert[b], Mary Philip[b], Hélène Martel[b], Alberto Riberi[f], Gilbert Habib[b], Didier Raoult[a,*]

- 2001-2011/2012-2017 prospektif çalışma
- 341 *S. aureus* İE;
- TMP-SXT&Clindamisin (171) // Kontrol (PE konvansiyonel) (170)
- TMP-SXT&Clindamisin koluna 7 gün PE yüksek doz(960/4800;1800/d); 5 hafta **std doz TMP_SXT PO**
- KK üreme uzun süreli (>48hr), apse ; rifampisin + genta eklenmiş

	T&C group n=171	Control group n=170	P	OR
Comorbidities				
Mean age in years (range)	64.4 (13–94)	59.4 (19–102)	0.007	
Male	115 (67.3%)	125 (73.5%)	0.23	
Prior IE	16 (9.4%)	13 (7.6%)	0.70	
Intravenous drug use	22 (12.9%)	26 (15.3%)	0.54	
HIV	3 (1.8%)	6 (3.5%)	0.34	
Diabetes	38 (22.2%)	30 (17.6%)	0.34	
Coronary artery disease	22 (12.9%)	18 (10.6%)	0.50	
Chronic lung injury	15 (9.1%)	18 (10.6%)	0.61	
Chronic renal failure	23 (13.5%)	27 (15.9%)	0.54	
Dialysis	7 (4.1%)	8 (4.7%)	0.80	
Elevated blood pressure	61 (35.7%)	42 (24.7%)	0.034	1.4 (1.03–2.1)
Alcohol	18 (8.8%)	11 (6.5%)	0.54	
Myocardial infarction	20 (11.7%)	18 (10.6%)	0.86	
Autoimmune disease	10 (5.8%)	6 (3.5%)	0.44	
History of cancer	18 (10.5%)	23 (13.5%)	0.41	
Leukaemia/lymphoma	5 (2.9%)	7 (4.1%)	0.41	
Charlson Comorbidity Index	3 (0–10)	3 (1–5)	0.27	
IE characteristics (non-exclusive)				
Native valve IE	97 (56.7%)	96 (56.5%)	1	
Valvular prosthesis IE	43 (25.1%)	34 (20.0%)	0.3	
Cardiac-device-related IE[a]	48 (28.1%)	48 (28.2%)	1	
Bicuspid valve	6 (3.5%)	8 (4.7%)	0.59	
MRSA	21 (12.3%)	19 (11.2%)	0.87	
Clinical features				
Fever[b]	134 (78.4%)	152 (89.4%)	0.007	0.88 (0.80–0.96)
Acute heart failure	38 (22.2%)	43 (25.3%)	0.53	
Cardiogenic shock	13 (7.6%)	7 (4.1%)	0.25	
Septic shock	24 (14.0%)	12 (7.1%)	0.051	
Heart murmur	65 (38.0%)	85 (50%)	0.029	0.76 (0.60–0.97)
Embolism	81 (47.4%)	94 (55.3%)	0.16	
Major cerebral bleeding	14 (8.2%)	21 (12.4%)	0.22	
Spondylodiscitis	19 (11.1%)	9 (5.3%)	0.074	
Mycotic aneurism	4 (2.3%)	12 (7.1%)	0.043	0.33 (0.11–1.00)
Echocardiographic features				
Aortic IE	57 (33.3%)	57 (33.5%)	1	
Mitral IE	51 (29.8%)	62 (36.5%)	0.13	
Tricuspid IE	37 (21.6%)	30 (17.6%)	0.41	
Cardiac-device-related IE	45 (26.3%)	48 (28.2%)	0.72	
Vegetation	[illegible]	[illegible]	[illegible]	[illegible]
Annular				
Pseudo				
Severe v				
Valvular				
Left ven				
Biological				
Leukocy				
C-reactiv				
Serum c				
Follow-up				
Relapse				
Recurre				
Persister				

Her iki kolda da aort ve mitral kapak tutulum oranları %33(29-36)

Outcome	Intention-to-treat analysis			On-treatment analysis		
	Control group n=170 (%)	T&C group n=171(%)	P	Control group n=126	T&C group n=138 (%)	P
Septic failure	14 (8.2)	10 (5.8)	0.41	6 (3.5)	3 (2.2)	0.02
Surgery	114 (67.1)	89 (52.1)	0.006	73 (57.9)	73 (52.9)	0.46
Relapses	22 (12.9)	13 (7.6)	0.11	13 (7.6)	8 (5.8)	0.6
Mean hospital stay (days)	34.1 ± 4.5	29.6 ± 3.9	0.14	32.2 ± 4.4	26.6 ± 4.1	0.06
Mean hospital stay alive (days)[a]	39.0 ± 5.2	29.8 ± 3.8	0.005	36.9 ± 4.8	26.4 ± 3.8	0.0007
In-hospital death	31/170 (18.2)	17/ 171 (9.9)	0.03	25/126 (14.7)	14/138 (10.1)	0.036
Sepsis/multi-organ failure	14 (45.2)	8 (47.1)	1	9 (36.0)	5 (35.7)	1
Other causes	17 (54.8)	9 (52.9)		16 (64.0)	9 (64.3)	
Death at day 30	24/169 (14.2)	12/169 (7.1)	0.05	19/125 (15.3)	10/136 (7.4)	0.05
Sepsis/multi-organ failure	10 (41.7)	5 (41.7)	1	6 (31.6)	3 (30.0)	1
Other causes	14 (58.3)	7 (58.3)		13 (68.4)	7 (70.0)	
Death at day 90	35/165 (21.2)	27/165 (16.4)	0.32	25/122 (20.5)	20/132 (15.0)	0.32
Sepsis/multi-organ failure	14 (40.0)	8 (29.6)	0.43	9 (36.0)	5 (25.0)	0.52
Other causes	21 (60.0)	19 (70.4)		16 (64.0)	15 (75.0)	
Global mortality[b]	51/170 (30.0)	33/171 (19.3)	0.024	37/126 (29.4)	28/138 (20.3)	0.11
One-year mortality	45/170	34/171	0.16	32/126	24/138	0.3

H. Tissot-Dupont, F. Gouriet and L. Oliver et al. / International Journal of Antimicrobial Agents xxx (xxxx) xxx

- Her iki kolda da aort ve mitral kapak tutulumları benzer
- Global mortalite , hastane mortalitesi ve 30 günlük mortalite ile hastanede kalış süresi TMP-SXT daha düşük

2019 sonrası

27th ECCMID Vienna, Austria 22 – 25 April 2017

Oral treatment of Infective Endocarditis

P. Muñoz, V. González-Ramallo, M.E. García Leoni, M. Valerio, A. Fernández-Cruz, B. Pinilla, M. Martínez-Sellés, G. Cuerpo, A. Vena, E. Bouza on behalf of Grupo de Apoyo a la Endocarditis Infecciosa del Gregorio Marañón (GAME).
Hospital General Universitario Gregorio Marañón

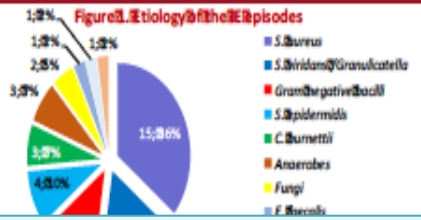
INTRODUCTION

- Outpatient Parenteral treatment (OPAT) of IE is being increasingly used, with very acceptable rates of hospital readmissions (10-26%) and relapses.
- However, information on oral treatment of infective endocarditis (IE), mainly left-sided, is very scarce.
- Oral drugs with excellent bioavailability are now available, which, theoretically could allow a

- Our goal
complet

- Setting:
inhabita
- The 435
Endocar
recorded
modified

Overall 10%
antimicrobi



Comparison of patients that received oral versus IV treatment

- Patients that received oral treatment had less comorbidities, received more valvular surgery and required more hospital re-admissions. (Table 1)
- Mortality at one-year follow up was similar in both groups.

Variables	Oral (N=44)	IV (N=391)	P
Age, median (IQR)	65 (50-76)	71 (58-78)	0.053
Sex (Male)	[illegible]	[illegible]	0.452
[illegible]	[illegible]	[illegible]	0.055
[illegible]	[illegible]	[illegible]	0.005
[illegible]	[illegible]	[illegible]	0.609
[illegible]	[illegible]	[illegible]	0.067
[illegible]	[illegible]	[illegible]	<0.01
[illegible]	[illegible]	[illegible]	0.399
[illegible]	[illegible]	[illegible]	0.067
[illegible]	[illegible]	[illegible]	0.279
[illegible]	[illegible]	[illegible]	0.752
[illegible]	[illegible]	[illegible]	0.035
[illegible]	[illegible]	[illegible]	0.268
[illegible]	[illegible]	[illegible]	0.273
[illegible]	[illegible]	[illegible]	0.019
[illegible]	[illegible]	[illegible]	0.092
[illegible]	[illegible]	[illegible]	<0.01
[illegible]	[illegible]	[illegible]	0.021
[illegible]	[illegible]	[illegible]	0.796
[illegible]	[illegible]	[illegible]	0.006
[illegible]	[illegible]	[illegible]	0.923
[illegible]	[illegible]	2 (0.5)	0.068
Readmission	15 (34.9)	48 (19.4)	0.022
One year mortality	2 (4.5)	23 (5.8)	0.984

435 hasta, prospektif kohort,
%34 aort, %38 mitral kapak tutulumu
En sık kullanılan AB;kinolon, SXT, LZD, rifampisin…
Tekrar hastaneye başvuru APAT ile benzer.
Oral tedavi güvenli

General characteristics of patients that received oral therapy

- Mean age was 59 years old (SD 21) and 30 patients (68%) were male.
- Etiology: *S. aureus* (15; 34%) predominated, followed by *S. viridans/ Granulicatella* spp. (7; 16) (Figure 1). Two patients had unknown etiology.
- Infection was mainly community-acquired (27; 61.4%).
- Infected sites were: native valves (22, 50%), prosthetic valves (13; 29.5%) and intra-cardiac material (9; 20.5%).

of other origin, spondylodiscitis, respiratory insufficiency, Leishmaniasis, pneumonia, bleeding, anticoagulation adjustment, tachycardia, neoplasia and heart transplantation (1 each).

- There were two early relapses (*Aspergillus* endocarditis and *S. viridans* IE), but those patients had left hospital early, against medical advice.
- One-year mortality was 4.5%, but none of the patients died because of the endocarditis.

CONCLUSIONS

- Our series suggests that it is safe and feasible to complete the treatment of selected complex episodes of endocarditis with outpatient oral regimes.
- The rate of readmissions is similar to patients treated with OPAT, and is not related to treatment failure.

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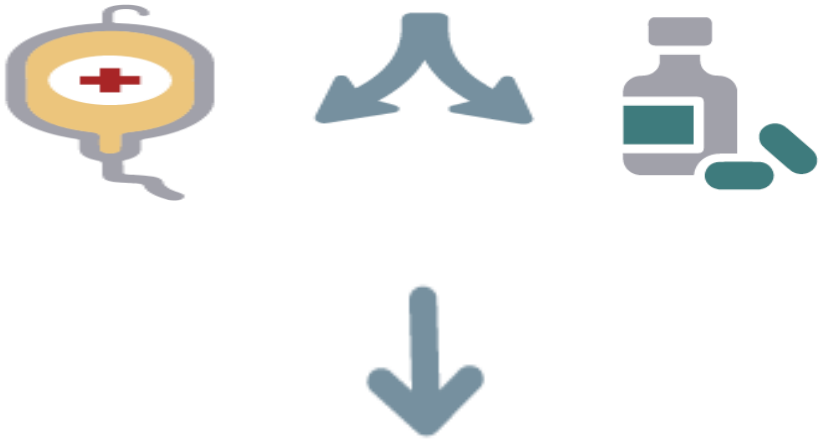
GAME Study Group: Emilio Bouza, Patricia Muñoz, Ana Fernández-Cruz, Maricela Valerio, Mercedes Marín, José Antonio García Robles, Rosa Ana López Jiménez, Ana González Morelle, Cristina Rincón, Antonia Delgado Montero, Víctor González Ramallo, Mª Eugenia García Leoni, Manuel Martínez Sellés, Eduardo Verde Moreno, Pilar Vázquez, Judith Sulis, Gregorio Cuerpo, Hugo Rodríguez Abella, Javier Hortal, Ángel Pinto, Daniel Celemín, Blanca Pinilla Llorente, Javier Bermejo.

2019 sonrası

RODEO 1 Çalışması (NCT02701608)

- Fransa, Çok merkezli, randomize, kontrollü, açık uçlu non inferiority
- 2016-2019, Çok ilaç duyarlı MSSA sol İE, 324 hasta, en az 10 gün PE tx

2015 ESC konvansiyonel



LVX+Rif

PRİMER SONLANIM NOKTASI

ClinicalTrials.gov

2019 sonrası

RODEO 2 Çalışması (NCT02701595)

- Fransa, Çok merkezli, randomize, kontrollü, açık uçlu non inferiority
- 2016-2021, Çok ilaç duyarlı Streptokok/enterokok sol İE, 324 hasta, en az 10 gün PE tx

2015 ESC konvansiyonel

Amoksisilin

PRİMER SONLANIM NOKTASI

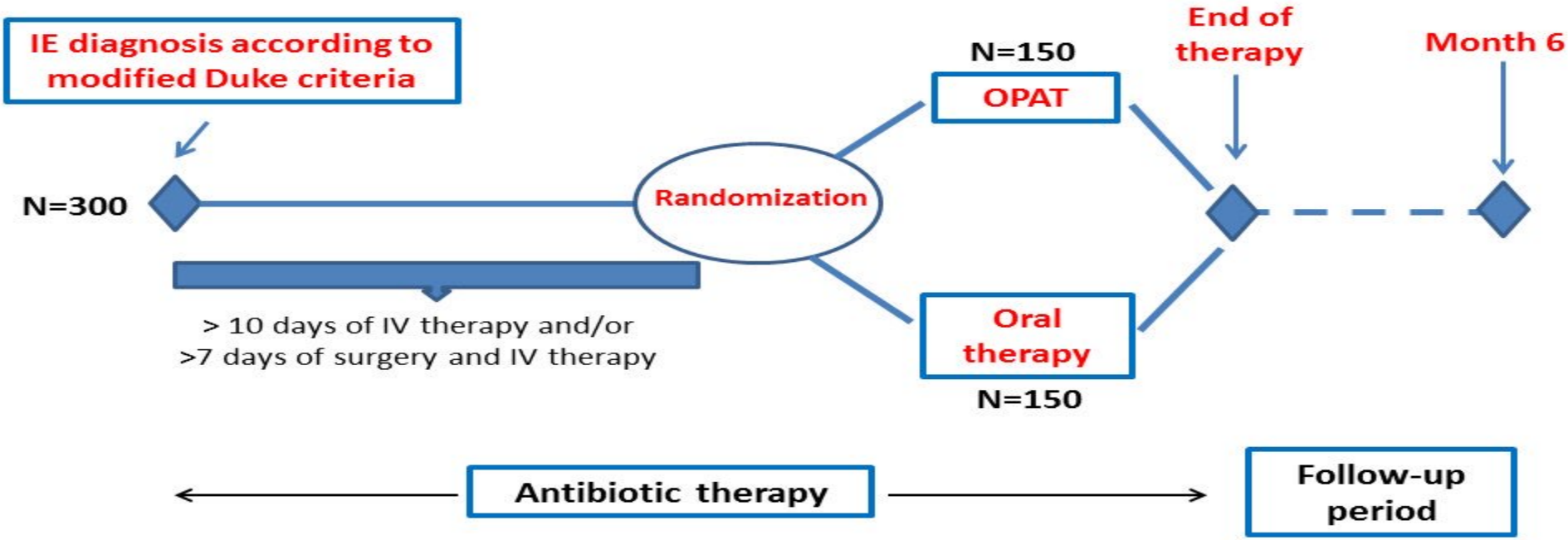
ClinicalTrials.gov

2019 sonrası

ORAL GEÇİŞ ve APAT karşılaştırması

Outpatient Oral *vs.* Parenteral Antimicrobial Therapy for IE trial (OraPAT-IE trial)

Investigator initiated, multicentre, open, non-inferiority randomized clinical trial



Ulusal Uzlaşı Raporu Ne Diyor?

- Sol kapak endokarditlerinde, infeksiyonun mortalite oranının yüksekliği ve oral tedavinin ülkemiz koşullarındaki yapılabilirliği ve etkinliği konusunda soru işaretleri olması nedeniyle tedavinin tümünün parenteral yoldan yapılması tercih edilmelidir.

Şimşek-Yavuz S *et al*. İnfektif Endokardit Ulusal Uzlaşı Raporu :
Klimik Derg. 2019; 32(Suppl. 1): 2-116

Ulusal Uzlaşı Raporu Ne Diyor?

- İV yol bulunamayan veya APAT yapılamayan, yabancı cisim veya komplikasyon bulunmayan duyarlı viridans streptokok endokarditlerinde, tedavinin ilk 2 haftası parenteral yoldan yapılmış olmak kaydıyla ve uyum ve takip sorunu yaşanmayacağından emin olunan hastalarda, tüm olası riskleri de içeren hasta bilgilendirmesi yapılıp, onam alındıktan sonra kalan tedavi süresi oral bir ajanla tamamlanabilir.

Türkiye Uzlaşı Raporu Ne Diyor?

- Oral tedaviye geçiş kararı "İnfektif Endokardit Ekibi"nin ortak kararıyla verilmelidir.

Şimşek-Yavuz S *et al*. İnfektif Endokardit Ulusal Uzlaşı Raporu :
Klimik Derg. 2019; 32(Suppl. 1): 2-116

Oral İdame tedavi uygulayamayacağımız hastalar?

- Dirençli bakteri infeksiyonları
- Nörolojik komplikasyon, kalp yetmezliği, metastatik septik odaklarla vb komplike olmuş İE olguları
- Vücut kitle indeksi > 40 olanlar
- İV tedavi gerektiren eşlik eden başka infeksiyon varlığı
- Bilgilendirilmiş onam veremeyenler

Abdominal hastalıklar nedeniyle oral tedavi sırasında emilimin azalacağından kuşku duyulanlar. Uyumu yetersiz olanlar

Şimşek-Yavuz S *et al*. İnfektif Endokardit Ulusal Uzlaşı Raporu :
Klimik Derg. 2019; 32(Suppl. 1): 2-116

Hangi hastalar?

- Penisiline duyarlı streptokoksik İE'li,
- Özellikle İV yol bulunamayan, APAT yapılamayan,
- Hastane yatış sorunları olan veya
- Toksisite veya alerji gibi nedenlerle alternatif bulunamayan hastalarda ,
- İlgili klinisyenlerin sorumluluğunda olmak üzere ve

hastaya tüm riskleri ve yararları anlatılarak

Şimşek-Yavuz S *et al*. İnfektif Endokardit Ulusal Uzlaşı Raporu :
Klimik Derg. 2019; 32(Suppl. 1): 2-116

Hangi Hastalar?

- Oral tedavinin süresi, doğal kapaklarda en az 2 hafta, yapay kapaklarda ise en az 4 hafta olmalıdır.

- Hastaların haftada 2- 3 kez poliklinikten muayenesi ve kontrolü sağlanmalıdır.

- Yönetimi “infektif endokardit ekibi” tarafından yapılmalıdır.

Şimşek-Yavuz S *et al*. İnfektif Endokardit Ulusal Uzlaşı Raporu :
Klimik Derg. 2019; 32(Suppl. 1): 2-116

Oral idame tedaviye geçilebilecek hastalar

- ≥ 18 yaş olanlar
- Duyarlı streptokoksik İE'si olanlar
- Toplamda en az 14 gün ve kapak cerrahisi uygulanmış olan hastalarda, cerrahiden sonra en az 1 hafta olacak şekilde parenteral uygun antibiyotik tedavisi almış olmak
- Vücut sıcaklığının en az 2 gündür < 38.0 °C olması
- İV antimikrobik tedaviyle CRP < 20 mg/l'ye, kan lökosit sayısınınsa <15.000/µl'ye düşmüş olması
- Oral tedaviye geçmeden 2 gün önce yapılmış TÖE'de veya ameliyat sırasında apse olmaması

Şimşek-Yavuz S *et al*. İnfektif Endokardit Ulusal Uzlaşı Raporu :
Klimik Derg. 2019; 32(Suppl. 1): 2-116

Hangi Antimikrobiyal?

- En az 14 günlük İV tedaviyi takiben
- amoksisilin 4X1gr/gün + rifampisin 2X600 mg/gün,

ardışık oral tedavisine geçilmesi düşünülebilir.

Siz sol kalp endokarditi olan hastanıza oral ardışık tedavi önerir miydiniz?

Teşekkürler…