

Yılın Ses Getiren Makaleleri-2016

Doç.Dr.Funda Şimşek

SB Okmeydanı Eğitim ve Araştırma Hastanesi

Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji

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1	Immunity	journal	16.215 Q1	311	239	719	9649	11663	684	17.62	40.37	
2	Lancet Infectious Diseases	journal	11.233 Q1	161	428	1002	8366	5580	279	20.04	19.55	
3	Clinical Microbiology Reviews	journal	8.741 Q1	205	34	109	9640	1970	104	16.24	283.53	
4	FEMS Microbiology Reviews	journal	7.587 Q1	150	52	149	9462	1891	136	13.52	181.96	
5	Trends in Microbiology	journal	5.285 Q1	150	114	299	6385	2219	254	7.96	56.01	

11	Trends in Parasitology	journal	3.193 Q1	115	100	256	5517	1380	218	6.57
12	AIDS	journal	3.112 Q1	188	261	1279	7216	4589	984	4.32
13	Emerging Infectious Diseases 	journal	3.023 Q1	175	530	1621	8796	6672	1050	6.41
14	Frontiers in cellular and infection microbiology 	journal	2.748 Q1	22	7	468	89	1837	442	4.24
15	Current Opinion in HIV and AIDS	journal	2.613 Q1	41	73	258	3681	938	239	4.20
16	Clinical Microbiology and Infection	journal	2.530 Q1	100	410	1028	9613	5036	940	4.62
17	Retrovirology 	journal	2.506 Q1	64	124	432	6252	1501	383	3.97
18	Journal of Acquired Immune Deficiency Syndromes	journal	2.434 Q1	127	421	1308	12256	3770	980	3.71

7	Neurobehavioral HIV Medicine 	journal	0.329 Q3	4	1	6	49	6	6	0.50	49.00	
8	VirusDisease	journal	0.329 Q3	8	45	202	1443	155	197	0.60	32.07	
9	Mycobiology 	journal	0.325 Q3	11	67	171	1837	149	158	0.72	27.42	
10	Indian Journal of Sexually Transmitted Diseases 	journal	0.313 Q3	9	57	117	733	55	82	0.49	12.86	
11	Journal of Preventive Medicine and Hygiene	journal	0.308 Q3	13	18	116	793	90	111	0.51	44.06	
12	Journal of Venomous Animals and Toxins Including Tropical Diseases 	journal	0.306 Q3	13	42	128	1200	131	120	1.45	28.57	
13	Jundishapur Journal of Microbiology 	journal	0.298 Q3	10	226	437	6521	346	422	0.86	28.85	
14	Japanese Journal of Antibiotics	journal	0.295 Q3	15	15	86	257	31	85	0.27	17.13	
15	Journal of AIDS and Clinical Research	journal	0.292 Q3	9	0	266	0	116	245	0.35	0.00	
16	Tropical Doctor	journal	0.283 Q3	26	68	220	817	112	208	0.46	12.01	

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Infectious Diseases



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1	Mikrobiyoloji Bulteni	journal	0.340 Q3	15	52	254	1258	181	250	0.73	24.19	
2	Turk hijiyen ve deneysel biyoloji dergisi. Turkish bulletin of hygiene and experimental biology	journal	0.133 Q4	2	41	81	1346	12	81	0.14	32.83	
3	Klimik Dergisi	journal	0.121 Q4	5	29	104	954	6	90	0.07	32.90	
4	Cocuk Enfeksiyon Dergisi	journal	0.120 Q4	4	45	144	668	16	101	0.17	14.84	

New England Journal of Medicine -
Dikkat çeken 13 yayın içinde 3 tane

NOTABLE ARTICLES OF 2016

A collection of important studies
from the past year as selected by NEJM editors

Original article-NEJM-2016

1 *Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older

* Preventing Shingles and Its Complications in Older Persons

2*Guillain-Barré Syndrome Associated with Zika Virus Infection in Colombia

3*Zika Getting on Your Nerves? The Association with the Guillain-Barré Syndrome

* Zika Virus in the Americas — Yet Another Arbovirus Threat

The Lancet Infectious Diseases-2016

- High-dose rifampicin, moxifloxacin, and SQ109 for treating tuberculosis: a multi-arm, multi-stage randomised controlled trial
- Association between Zika virus infection and microcephaly in Brazil, January to May, 2016: preliminary report of a case-control study
- Infectious disease emergencies: taking the long-term view
- New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective
- New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective

ECCMID 2016

The Year in Infectious Diseases (Part II)

- Skin abscess (1)
- CAP (2)
- Intraabdominal infection (1)
- Intravascular catheter-related infection (1)
- Antibiotic therapy for MRSA (2)
- Tuberculous meningitis (1)

Review period: April 2015 – March 2016

NEJM 4; LANCET 2; BMJ 1, CID 1



Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin



Short report

Healthcare-associated Gram-negative bloodstream infections: antibiotic resistance and predictors of mortality

Ö. Ergönül^{a,*}, M. Aydın^b, A. Azap^c, S. Başaran^d, S. Tekin^a, Ş. Kaya^e, S. Gülsün^e, G. Yörük^f, E. Kurşun^g, A. Yeşilkaya^h, F. Şimşekⁱ, E. Yılmaz^j, H. Bilgin^k, Ç. Hatipoğlu^l, H. Cabadak^m, Y. Tezer^m, T. Toganⁿ, İ. Karaoglan^o, A. İnan^p, A. Engin^q, H.E. Alışkan^g, S.Ş. Yavuz^d, Ş. Erdinç^l, L. Mulazimoglu^k, Ö. Azap^h, F. Can^a, H. Akalın^j, F. Timurkaynak^b, Turkish Society of Clinical Microbiology and Infectious Diseases, Healthcare-Related Infections Study Group

Giriş

- Sağlık bakımı ile ilişkili infeksiyonlar(SBİİ) önemli bir mortalite ve morbidite nedenidir.
- SBİİ arasında kan dolaşımı infeksiyonları(KDİ) yüksek mortalite oranı ile birlikte,dir,
- Gram negatif bakterilere (GNB) bağlı KDİ mortalite oranları daha yüksek,
- GNB-KDİ'nda tedavi seçenekleri sınırlı,
- Karbapenem dahil birçok antibiyotik grubuna dirençli
- Global olarak artan öneme sahip,

Giriş

- Karbapenem direnç oranları *Acinetobacter* %87*,
Pseudomonas %34 *

Klinik ve mikrobiyolojik verilerin toplandığı bir çalışmanın ülkemizde sağlık bakımı ile ilişkili gram negatif kan dolaşımı infeksiyonlarında büyük resmi görmek için gerekli olduğu

- *National nosocomial infections surveillance network of Turkey 2013 report; Halk Sağlığı 2015

Metod

- Retrospektif, çok merkezli
 - 7 farklı coğrafik bölgeden 17 merkez
 - 1-31 Ocak 2013 arasındaki hastalar
 - CDC kriterlerine göre çalışmaya dahil edildi.
-
- En yaygın kullanılan ampirik antibiyotikler; Piperasilin-tazobaktam ve karbapenem %68

Metod

- CDC kriterlerine göre tanımlanmış, klinik olarak anlamlı kabul edilen kan kültürleri çalışmaya dahil edildi,
- İdentifikasyon  otomatize sistemler (VITEK2, Phoenix)
- Antibiyotik duyarlılık testleri  disk diffüzyon, MİK
- Karbapenem(ertapenem, meropenem, imipenem),
- 3. ve 4. kuşak sefalosporinler(seftriakson,seftazidim, sefepim)
- Kinolonlar
- Aminoglikozid(amikasin, gentmisin)
- Kolistin

Table I
Univariate analysis of risk factors for mortality in patients with healthcare-associated Gram-negative bloodstream infections

Variable	Patients who died N=371	Patients who survived N=460	P-value
Mean age (SD)	60 (19)	54 (18)	<0.001
Female	185 (50)	192 (42)	0.019
Primary diagnosis			
Solid organ tumours	72 (20)	79 (17)	
Haematological malignancies	48 (13)	99 (22)	
Neurological diseases	53 (14)	61 (14)	
Trauma	32 (9)	36 (8)	
Cardiovascular diseases	41 (11)	37 (8)	
Pulmonary diseases	56 (15)	41 (9)	
Renal diseases	7 (2)	22 (5)	
On intensive care unit	287 (77)	213 (46)	<0.001
Operation within one month	132 (32)	172 (39)	0.567
Antibiotic use within last three months	228 (68)	277 (65)	0.5
Primary bacteraemia	216 (59)	266 (58)	0.902
Ventilator-associated pneumonia	155 (43)	100 (22)	<0.001
Central venous catheter	307 (84)	262 (58)	<0.001
Mean time to first positive blood culture after admission (days)	20	23	0.091
Mean C-reactive protein level	132	126	0.409
Mean leukocyte count	13117	11317	0.04
Mean procalcitonin level	11	10	0.796
Mean time for starting appropriate antibiotic (days)	2	2	0.94
Antibiotic resistance			
Carbapenem resistance	236 (62)	143 (37)	<0.001
Fluoroquinolone resistance	187 (78)	172 (62)	<0.001
Third-generation cephalosporin resistance	238 (89)	211 (71)	<0.001
Aminoglycoside resistance	115 (49)	88 (33)	<0.001

SD, standard deviation.

Istatistik

- Student's t test ;
- Chisquared test
- Multivariate analiz,
- STATA v11
- $P < 0.05$

Sonuçlar

- 831 vaka çalışmaya alındı, 371(%44)'i fatal
- Ortalama yaş ve lökosit sayısı fatal olgularda yüksek,

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SD, standard deviation.

Sonuçlar

- *Acinetobacter baumannii* 256(%31)
- *Klebsiella pneumoniae* 221(%27)
- *E.coli* 202(%24)
- *Pseudomonas aeruginosa* 74(%9)
- *Enterobacter cloacea* 32(%4)
- *Stenotrophomonas maltophilia* 15(%1.5)
- *Serratia marcencens* 12(%1.59)
- *Proteus sp*, *Burkholderia cepacia*,
- Diğer
- En yüksek antibiyotik direnci *Acinetobakter*'de

Table II

Antibiotic resistance rates in healthcare-associated Gram-negative bloodstream infections

Bacteria	Carbapenem N (%)	Fluoroquinolones N (%)	Third-generation cephalosporins N (%)	Aminoglycosides N (%)	Colistin N (%)
<i>Acinetobacter baumannii</i>	239 (94)	240 (94)	247 (97)	187 (73)	15 (6)
<i>Klebsiella pneumoniae</i>	88 (40)	130 (60)	159 (72)	56 (25)	14 (6)
<i>Escherichia coli</i>	13 (6.4)	128 (63)	143 (71)	47 (23)	0
<i>Pseudomonas aeruginosa</i>	32 (43)	36 (49)	37 (51)	19 (26)	1 (1)
<i>Enterobacter cloacae</i>	5 (16)	6 (19)	16 (53)	5 (16)	0

Table III

Multi-variate analysis of risk factors for mortality in patients with healthcare-associated Gram-negative bloodstream infections

Variable	Odds ratio	95% CI	<i>P</i> -value
Age >70 years	2	1.22–3.51	0.006
Central venous catheter	2.1	1.09–4.07	0.025
Ventilator-associated pneumonia	1.9	1.1–3.16	0.02
Carbapenem resistance	1.8	1.11–2.95	0.016
APACHE II score	1.1	1.07–1.13	<0.001

CI, confidence interval.

Sonuçlar

- Vaka- fatalite oranı; %44
- Kaye ve ark. çalışması ile benzer(%49)
- >70 yaş  mortalite için anlamlı
- Komorbid durumlar
- VIP ve SVK kullanımı yüksek,
- Vaka-fatalite oranı *Acinetobacter baumannii* için %62

Sonuçlar

- Acinetobakter'de Karbapenem direnci ;
- Bizim çalışmamızda %94,
- Finlandiya-Norveç %0,
- Yunanistan %90

Sonuçlar

- Karbapenem direnci mortalite için bağımsız risk faktörü
- Ventilatör ve SVK; enfeksiyon kontrolünde dikkat edilmeli,
- Antibiyotik kullanım stratejileri iyi belirlenmeli,
- Ülkemizdeki durumu görmek için anlamlı
- GNB yayılımı iyi enfeksiyon kontrol önlemleri, etkin antibiyotik politikaları ile önlenmelidir.

ORIGINAL ARTICLE

Intensified Antituberculosis Therapy in Adults with Tuberculous Meningitis

A. Dorothee Heemskerk, M.D., Nguyen D. Bang, Ph.D., Nguyen T.H. Mai, Ph.D.,
Tran T.H. Chau, Ph.D., Nguyen H. Phu, Ph.D., Pham P. Loc, M.D.,
Nguyen V.V. Chau, Ph.D., Tran T. Hien, Ph.D., Nguyen H. Dung, Ph.D.,
Nguyen T.N. Lan, Ph.D., Nguyen H. Lan, M.D., Nguyen N. Lan, M.D.,
Le T. Phong, M.D., Nguyen N. Vien, M.D., Nguyen Q. Hien, M.D.,
Nguyen T.B. Yen, M.D., Dang T.M. Ha, Ph.D., Jeremy N. Day, F.R.C.P.,
Maxine Caws, Ph.D., Laura Merson, B.S., Tran T.V. Thinh, M.D.,
Marcel Wolbers, Ph.D., Guy E. Thwaites, F.R.C.P., and Jeremy J. Farrar, F.R.C.P.

Giriş

- Tüberküloz tedavisinde kullanılan standart tedavi ve kortikosteroid tedavisi ölüm oranını azaltmaktadır
- Hastalık hem ölüme neden olması hem de hastaların neredeyse yarısında sakatlık bırakması açısından önemini korumaktadır.
- Tbc tedavisinde standart tedavi 4 lü tedavidir.
- Anti tbc ilaçların beyine farklı penetrasyon yetenekleri mevcuttur.

Giriş

- Rifampisin tbc tedavisinde kritik ilaçtır.
- BOS konsantrasyonu plazma konsantrasyonundan %30 daha az,
- Oral rifampisin dozu 10 mg/kg  13 mg/kg

- Kabul edilebilir yan etki , plazma kons da %65 artış*
- Kinolonlar; tbc tedavisinde kullanılır
- KBB ne iyi penetrasyonu iyi , plazma kons nun %70 i

• * Ruslami R et al. Pharmacokinetics and tolerability of a higher rifampin dose versus the standard dose in pulmonary tuberculosis patients. Antimicrob Agents Chemother 2007; 51: 2546-51.

Amaç

- Yoğun antitbc tedavi alan hastalarda standart tedavi alan hastalara göre tbc menenjitten ölüm oranlarında azalma olup olmadığının belirlenmesi

Randomize , çift kör, plasebo kontrollü, Vietnam'da iki merkez
Nisan 2011- Haziran 2014

Çalışma grubu 817 hasta (349 u HIV ile infekte)

- >18 yaş,
- Klinik olarak Tbc menenjit tanısı konan (>5 gün menenjit semptomları olan, ense sertliği, anormal BOŞ bulguları
- Konsensus vaka tanımlamasına göre ; definitive, probable, possible, unlikely tbc menenjit
- Max skor 20, <6 ise unlikely
- İlaç direnci: sadece INH R ise: INH: R, R :H
- MDR için: INH-R, diğer ilaçlar

Çalışma dışı bırakılan grup

- >7 günden fazla anti tbc tedavi alan,
- Gebelik , hipersitivite, kinolon, rifampinlere reak ,
- Önceden MDR tbc geçirme öyküsü olan, kreatinin ve bilirubin yüksekliği olan hastalar

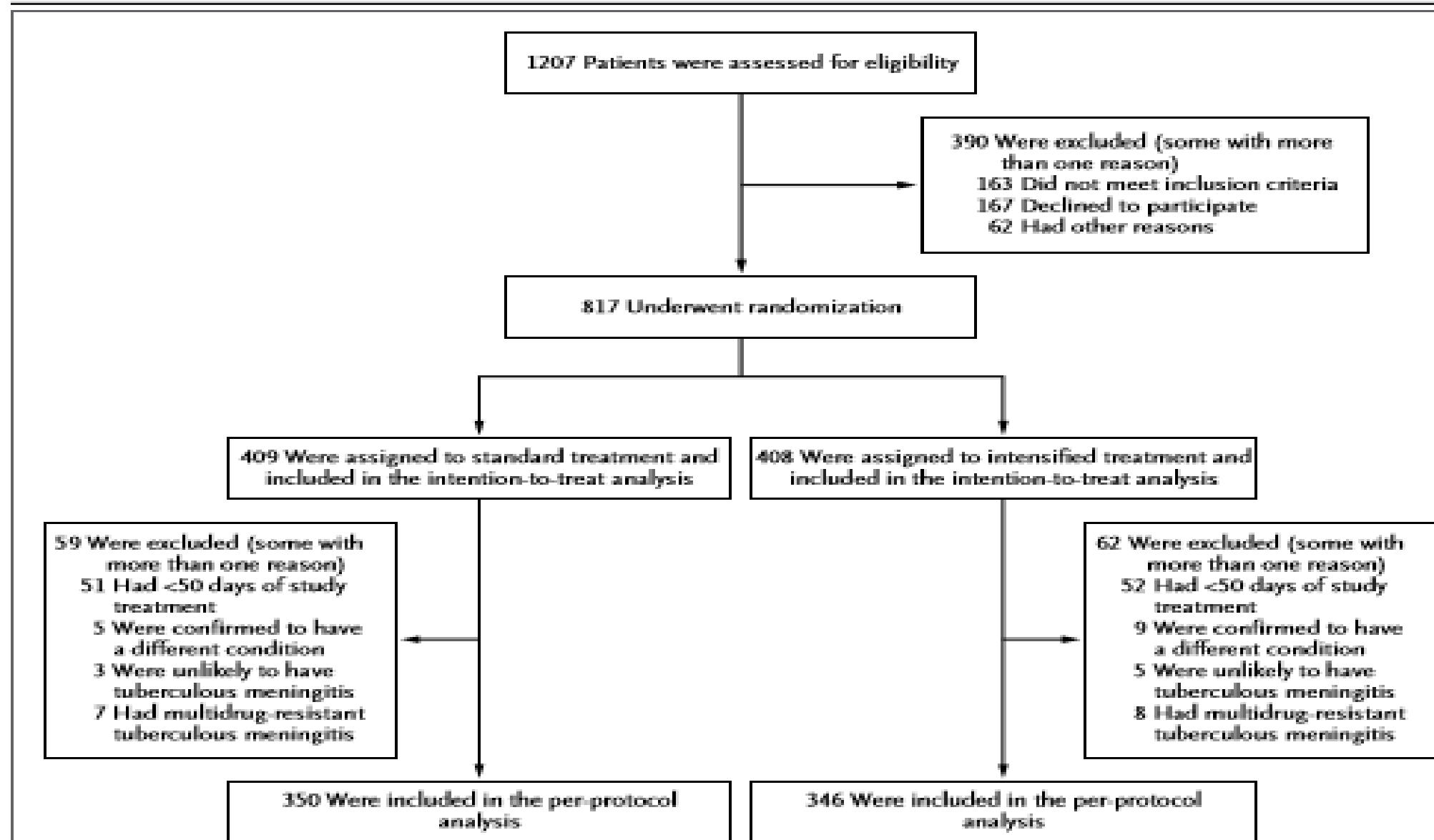
Tedavi Grupları

3 ay INH+R+E+P, 6 ay INH+R

- INH 5 Mg/kg/gün - maksimum 300mg
- Rifampin 10mg/kg /gün,
- Pyrazinamide 25mg/kg/gün- maksimum 2 g
- Ethambutol 20 mg/kg/gün- maksimum-1.2 g
- Dexamethasone 6 - 8 hafta

2 ay INH+R+E+P, 7 ay INH+R

- INH 5 Mg/kg/gün -maksimum 300mg
- Rifampin 15 mg/kg /gün,
- Pyrazinamide 25mg/kg/gün- maksimum 2 g
- Ethambutol 20 mg/kg/gün- maksimum-1.2 g
- Streptomycin 20 mg/kg- maximum, 1 g
- Levofloksasin 20mg/kg/gün
- Dexamethasone 6 - 8 hafta



Metod

- BOS ; boyama- kültür ,
- CSF - Xpert MTB/RIF test
- INH, R, ETM, STREP - mycobacterial growth indicator tube
- HCV, HIV, CD4

Table 1. Characteristics of the Patients at Enrollment.*

Characteristic	Standard Regimen (N = 409)	Intensified Regimen (N = 408)	All Patients (N = 817)
Male sex — no. (%)	278 (68.0)	282 (69.1)	560 (68.5)
Median age (IQR) — yr	35 (30–47)	35 (29–45)	35 (29–46)
MRC grade — no. (%)†			
1	160 (39.1)	158 (38.7)	318 (38.9)
2	178 (43.5)	179 (43.9)	357 (43.7)
3	71 (17.4)	71 (17.4)	142 (17.4)
HIV-infected — no. (%)	174 (42.5)	175 (42.9)	349 (42.7)
Median CD4 count (IQR) — cells/mm ³ ‡	38 (15–82)	38 (14–113)	38 (14–101)
Diagnostic category — no. (%)§			
Definite tuberculous meningitis	201 (49.1)	206 (50.5)	407 (49.8)
Probable tuberculous meningitis	109 (26.7)	105 (25.7)	214 (26.2)
Possible tuberculous meningitis	91 (22.2)	83 (20.3)	174 (21.3)
Unlikely to be tuberculous meningitis	3 (0.7)	5 (1.2)	8 (1.0)
Confirmed other condition	5 (1.2)	9 (2.2)	14 (1.7)
Resistance category			
Drug-susceptibility test results available — no.	156	166	322
No isoniazid or rifampin resistance — no. (%)¶	107 (68.6)	113 (68.1)	220 (68.3)
Isoniazid monoresistance — no. (%)	41 (26.3)	45 (27.1)	86 (26.7)
Rifampin monoresistance — no. (%)	1 (0.6)	0	1 (0.3)
Multidrug resistance — no. (%)	7 (4.5)	8 (4.8)	15 (4.7)

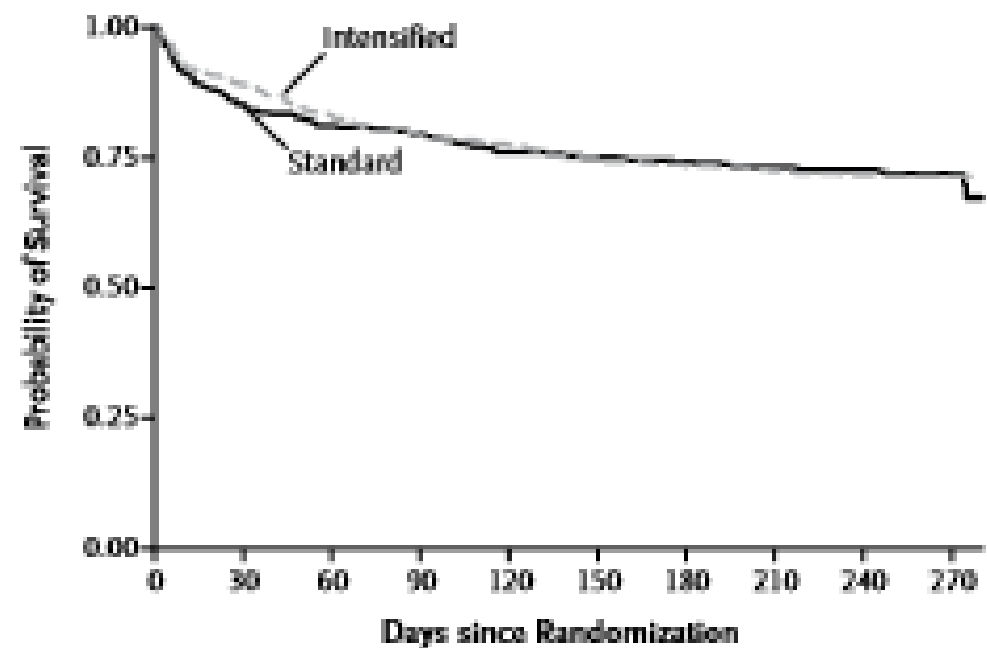
*Numbers in parentheses indicate the percentage of patients in each category. †MRC grade 1 indicates mild disease, grade 2 indicates moderate disease, and grade 3 indicates severe disease. ‡Values are median and interquartile range. §Values are number and percentage of patients. ¶Values are number and percentage of patients with drug-susceptibility test results available.

Table 2. Survival during the 9-Month Study Period.

Subgroup	Standard Regimen (N=409) <i>no. of deaths/total no. of patients</i>	Intensified Regimen (N=408) <i>no. of deaths/total no. of patients</i>	Hazard Ratio (95% CI)	P Value	P Value for Heterogeneity*
Intention-to-treat population	114/409	113/408	0.94 (0.73–1.22)	0.66	
Per-protocol population	94/350	93/346	0.91 (0.68–1.21)	0.52	
MRC grade					0.69
1	25/160	21/158	0.82 (0.46–1.46)	0.49	
2	50/178	52/179	1.07 (0.72–1.57)	0.74	
3	39/71	40/71	0.87 (0.56–1.36)	0.55	
HIV infection status					0.74
Uninfected	46/235	45/233	1.00 (0.66–1.51)	1.00	
Infected†	68/174	68/175	0.91 (0.65–1.27)	0.57	
Previous tuberculosis					0.82
No	89/347	78/324	0.91 (0.67–1.23)	0.53	
Yes	25/62	35/84	0.99 (0.59–1.67)	0.97	
Receiving antituberculosis treatment at enrollment‡					0.02
No	36/150	49/149	1.38 (0.89–2.12)	0.15	
Yes	78/259	64/259	0.74 (0.53–1.03)	0.07	
Diagnostic category§					0.93
Definite tuberculous meningitis	56/201	55/206	0.90 (0.62–1.31)	0.57	
Probable tuberculous meningitis	30/109	33/105	1.10 (0.66–1.83)	0.71	
Possible tuberculous meningitis	28/91	25/83	0.94 (0.54–1.63)	0.82	
Resistance category					0.04
No or other resistance	22/107	30/113	1.54 (0.88–2.71)	0.13	
Isoniazid resistance	16/41	11/45	0.45 (0.20–1.02)	0.06	
Rifampin or multidrug resistance	6/8	5/8	0.63 (0.15–2.69)	0.53	

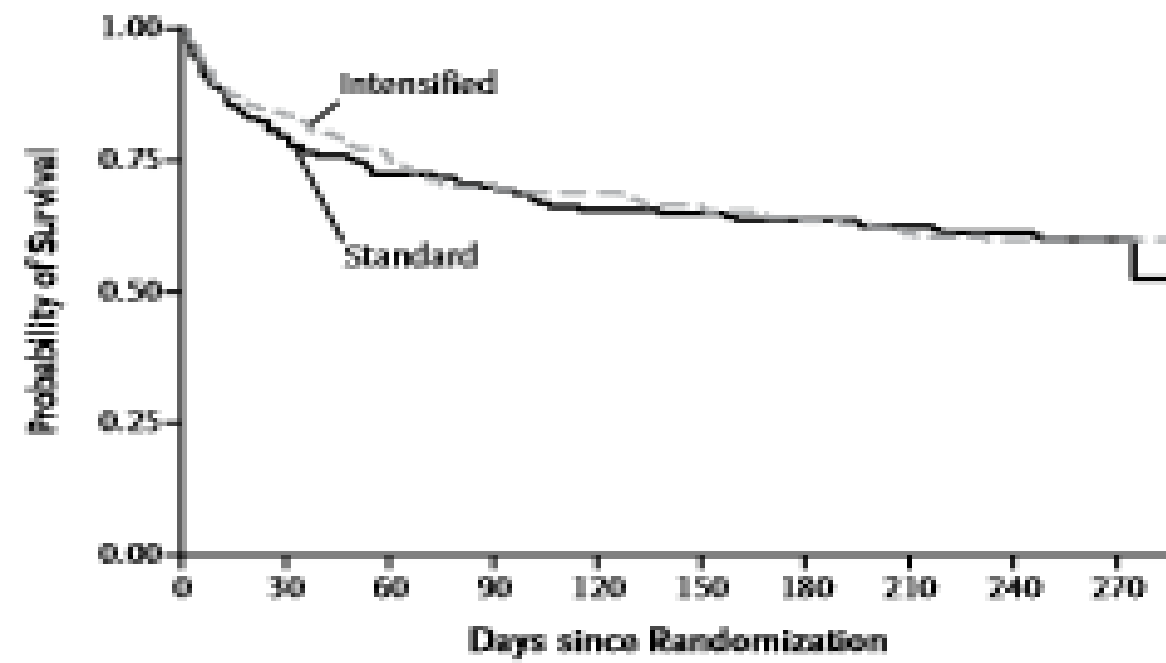
* Heterogeneity was tested with a likelihood ratio test for an interaction term between the subgroup variable and the randomly assigned treatment.

A All Patients



No. at Risk										
Standard	409	342	322	315	298	293	290	286	284	222
Intensified	408	353	328	313	305	295	288	283	379	225

C HIV-Infected Patients



No. at Risk										
Standard	174	134	120	115	106	104	102	100	98	71
Intensified	175	142	128	118	116	112	106	102	100	77

Tartışma

- Yoğun antitbc tedavi ile standart tedavi arasında anlamlı fark bulunamamış,
- Sonuçlar önceki çalışmalarla çelişiyor,
- 15 mg/kg/gün oral Rifampin dozu yeterli intraserebral ilaç konsantrasyonuna ulaşamadığından bakterinin ölmesi için yeterli değil.
- Son çalışmalarda çok daha yüksek dozlar (35 mg/kg/gün) güvenli olarak bildirilmiş

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High-dose rifampicin, moxifloxacin, and SQ109 for treating tuberculosis: a multi-arm, multi-stage randomised controlled trial

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- Randomize, kontrollü
- Güney Africa ve Tanzania, 7 ayrı ünite,
- Yeni tanı, rifampisin hassas, daha önce pulmoner tbc tedavisi almamış,
- 35 mg/kg rifampicin/gün, 15-20 mg/kg ethambutol,
- 20 mg/kg rifampicin/gün, 400 mg moxifloxacin,
- 20 mg/kg rifampicin/gün, 300 mg SQ109,
- 10 mg/kg rifampicin/gün 300 mg SQ109, veya
- Standard tedavi (10 mg/kg rifampicin, 5 mg/kg isoniazid, 25 mg/kg pyrazinamide, and 15-20 mg/kg ethambutol.

Sonuç

- Rifampisin 35 mg/kg/gün güvenli
- reduced the time to culture conversion in liquid media, and could be a promising component of future, shorter regimens. Our adaptive trial design was successfully implemented in a multi-centre, high tuberculosis burden setting, and could speed regimen development at reduced cost.

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RESEARCH

**Rapid Detection of Polymyxin
Resistance in *Enterobacteriaceae***

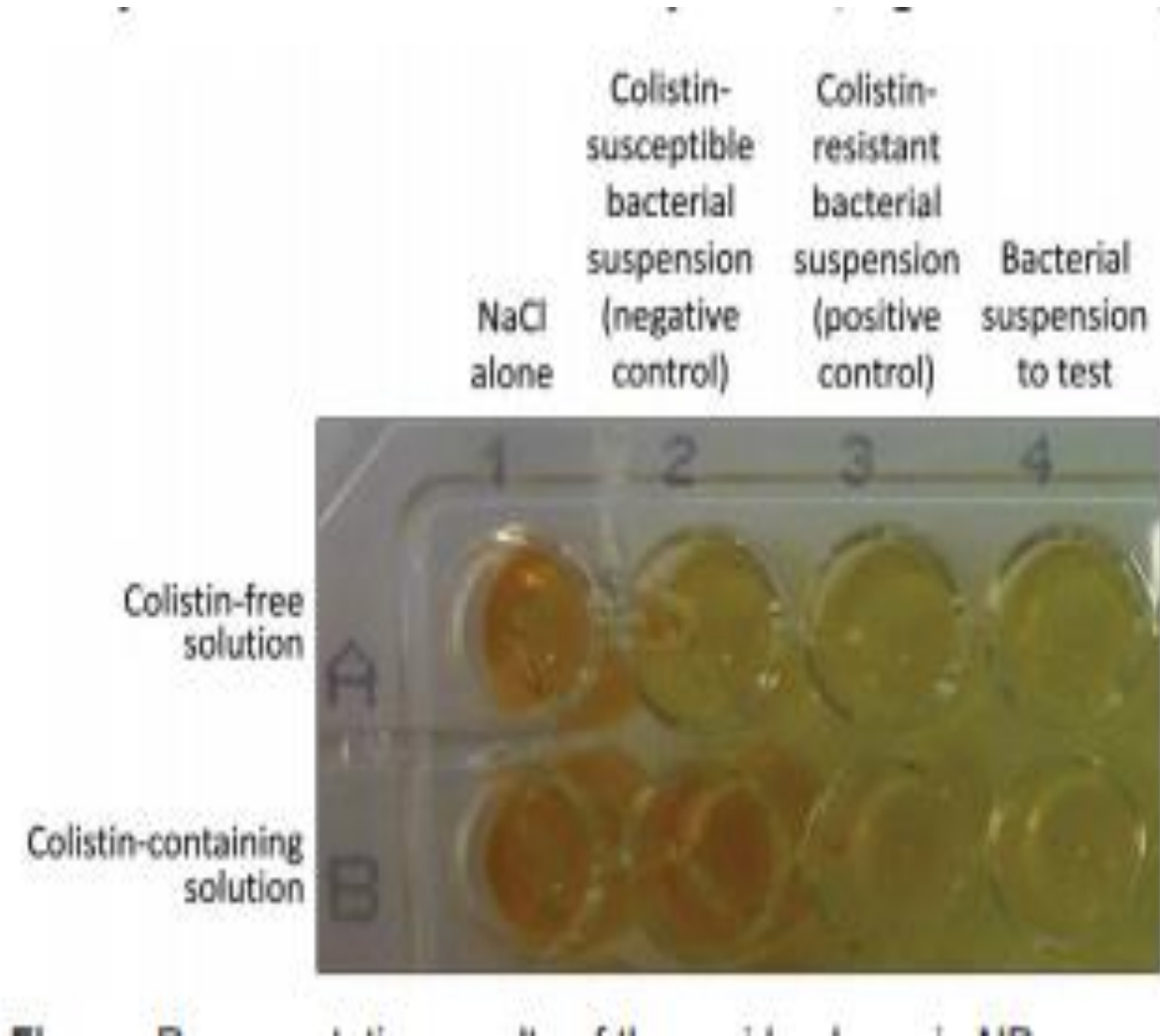
Patrice Nordmann, Aurélie Jayol, Laurent Poirel

Giriş

- Karbapenemaz üreten Enterobacteriaceae klinik olarak en önemli çoğul dirençli bakteriler arasında yer alır . Artan kolistin kullanımı kullanımı kazanılmış kolistin direncini artırmaktadır.
- Polimiksin direncini saptamada standart referans teknik broth microdilüsyon
- Sonuçlanma süresi 24 saat, çalışılması zahmetli
- Diğer teknikler disk difüzyon ve E test, sonuçlanma süresi 18-24 saat,
- Polimiksin molekülünün zayıf difüzyonundan dolayı testlerde yalancı pozitiflik oranı yüksek(%32).

Rapid polymyxin NP -Nordmann/Poirel test

- Polimiksinin belli konsantrasyonlarında bakteriyel üremenin olup olmadığını saptıyor,
- Bakterinin karbonhidrat metabolizması üzerinden indikatörle oluşan renk değişikliği temeline dayanıyor.



Materyal-Metod

- 200 örnek, 135 Enterobacteriaceae polimiksine dirençli,
- 5 'i intrinsik polimiksin dirençli türler (*Morganella morganii*, *Proteus mirabilis*, *Proteus vulgaris*, *Providencia stuartii*, and *Serratia marcescens*)
- 130 izolat (*Klebsiella* spp., *E. coli*, *Enterobacter* spp., *Hafnia alvei*) kazanılmış polimiksin direnci olan
- 1 heterorezistan ,kolistin MIC 'i yüksek *Klebsiella pneumoniae*

Sonuç

- Rapid Polymyxin NP testi ile saptanan kolistin direnç sonuçları uyumlu bulunmuş.
- Sensitivite 99.3%
- Specifite 95.4%

Tartışma

- Rapid polymyxin NP test kolay uygulanır, hızlı (6 saat), duyarlılığı yüksek,
- Enfeksiyon kontrol önlemlerine katkı sağlar,
- karbapenemaz üreten bakterilerin endemik olarak görüldüğü bölgelerde polimiksin duyarlılığı ya da direnci ile ilgili bilgi verir.
- Çalışmada bildirilen kısıtlılıklar; Heterorezistan izolatların polimiksin duyarlılığı ile ilgili yeterli veri yok,
- Polimiksin dirençli *Pseudomonas aeruginosa* ve *Acinetobacter baumannii* ile ilgili çalışma yok,
- Oluşan renk değişikliğini deneyimli personel değerlendirmeli.

Combination of Vancomycin and β -Lactam Therapy for Methicillin-Resistant *Staphylococcus aureus* Bacteremia: A Pilot Multicenter Randomized Controlled Trial.

Davis JS¹, Sud A², O'Sullivan MV³, Robinson JO⁴, Ferguson PE⁵, Foo H⁶, van Hal SJ⁷, Ralph AP⁸, Howden BP⁹, Binks PM¹⁰, Kirby A¹¹, Tong SY⁸; [Combination Antibiotics for Methicillin Resistant Staphylococcus aureus \(CAMERA\) study group](#); [Australasian Society for Infectious Diseases Clinical Research Network](#).

⊕ Collaborators (32)

⊕ Author information

Abstract

BACKGROUND: In vitro laboratory and animal studies demonstrate a synergistic role for the combination of vancomycin and antistaphylococcal β -lactams for methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia. Prospective clinical data are lacking.

METHODS: In this open-label, multicenter, clinical trial, adults with MRSA bacteremia received vancomycin 1.5 g intravenously twice daily and were randomly assigned (1:1) to receive intravenous flucloxacillin 2 g every 6 hours for 7 days (combination group) or no additional therapy (standard therapy group). Participants were stratified by hospital and randomized in permuted blocks of variable size. Randomization codes were kept in sealed, sequentially numbered, opaque envelopes. The primary outcome was the duration of MRSA bacteremia in days.

RESULTS: We randomly assigned 60 patients to receive vancomycin (n = 29), or vancomycin plus flucloxacillin (n = 31). The mean duration of bacteremia was 3.00 days in the standard therapy group and 1.94 days in the combination group. According to a negative binomial model, the mean time to resolution of bacteremia in the combination group was 65% (95% confidence interval, 41%-102%; P = .06) that in the standard therapy group. There was no difference in the secondary end points of 28- and 90-day mortality, metastatic infection, nephrotoxicity, or hepatotoxicity.

CONCLUSIONS: Combining an antistaphylococcal β -lactam with vancomycin may shorten the duration of MRSA bacteremia. Further trials with a larger sample size and objective clinically relevant end points are warranted. Australian New Zealand Clinical Trials Registry:

ACTRN12610000940077 (www.anzctr.org.au).

- Amaç: MRSA bakteremisinde, vankomisin beta laktam antibiyotikle kombinasyonunun tek başına vankomisin kullanımından daha etkin olduğu hipotezini desteklemek,
- Metod: Çok merkezli ,pilot, klinik çalışma
Ocak 2011- Mayıs 2014, 7 hastane, 60 hasta

7 gün süreyle

Vankomisin 1.5 g iv/2x1/7 gün - 29 hasta veya

Vankomisin 1.5 g iv/2x1 ve floksasilin 2g iv /4x1 -31 hasta

- **Sonuç:** 28 ve 90 günlük mortalite , metastatik infeksiyon, nefrotoksisite veya hepatotoksisite açısından anlamlı fark bulunamamış.

- Teşekkür ederim