ESBL Salgılayan Kökenlerle Gelişen Üriner Sistem Olgusunda Tedavi

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İnf. Hst. ve Kl. Mik. Srv - Istanbul

Sunum Planı

- Olgu sunumu
- Olguların değerlendirilmesi
- Epidemiyolojik veriler
- Tanı ve tedavi yaklaşımları
- Ülkemiz açısından sorunun boyutu
- Güncel veriler ışığında genel yaklaşım

Olgu 1

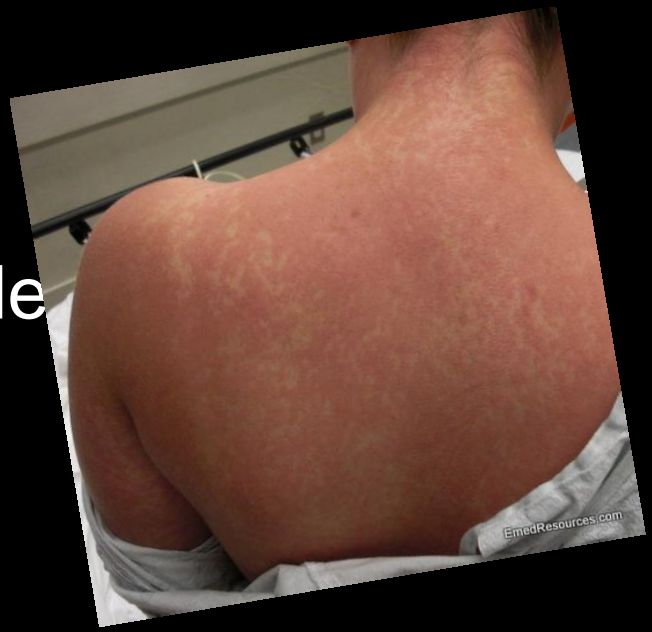
- 33 yaşında kadın hasta, evli ve iki çocuklu
- İdrar yaparken yanma ve sık idrara çıkma
- Yakınmaları son iki gündür mevcut..
- Bir yıl önce benzer şikayetleri nedeniyle üç günlük TMP/SMX tedavisi kullanmış
- Bilinen başka bir hastalığı bulunmuyor.

Laboratuar Bulguları

- Beyaz Küre: 7800 / mm3
- Sedimentasyon: 8 mm/saat
- CRP: 2.8 mgr/L (0-5)
- Tam idrar:
  - Nitrit testi (+)
  - Her sahada 7-8 BK, 2-3 eritrosit

Tedavi

- TMP/SMX (800/160 mg tb) 2x1 başlandı
- İkinci gün boyun ve sırt bölgesinde hassasiyet ve kızarıklık
- Siprofloksasin (500 mg tb) 2x1



TEDAVİDEN 10 GÜN SONRA
SIK İDRARA ÇIKMA
İDRAR YAPARKEN YANMA..

İdrar Kültürü

- *Escherichia coli* > 100.000 cfu/mL

Antibiyotikler	Duyarlı	Dirençli
Ampisilin		+
Amoksilin Klavulonat	+	
Sefuroksim		+
Sefotaksim		+
Seftriakson		+
Sefepim		+
Piperasilin/Tazobaktam	+	
Siprofloksasin		+
TMP/SMX		+
Amikasin	+	
Ertapenem	+	
İmipenem	+	

İdrar Kültürü

GSBL (+) *Escherichia coli*

Olgu 2

- 49 yaşında kadın hasta,
- Evli ve bir çocuklu
- Ateş,
- Yan ağrısı,
- Bulantı-kusma
- Sık idrara çıkma,
- İdrar yaparken yanma..
- Altı ay önce geçirilmiş Üriner Sistem İnf.

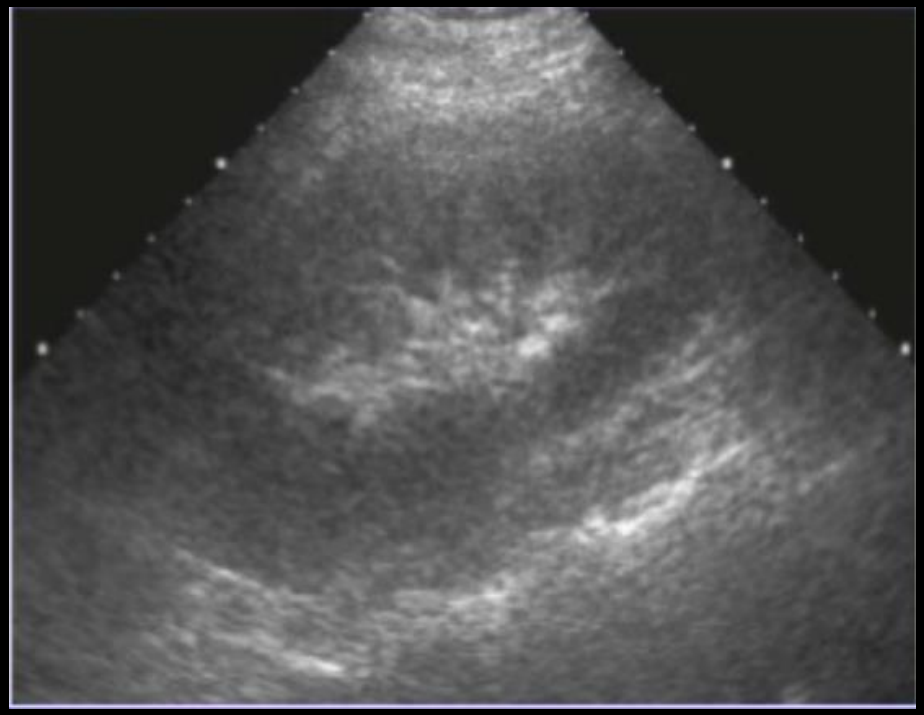
Fizik Muayene Bulguları

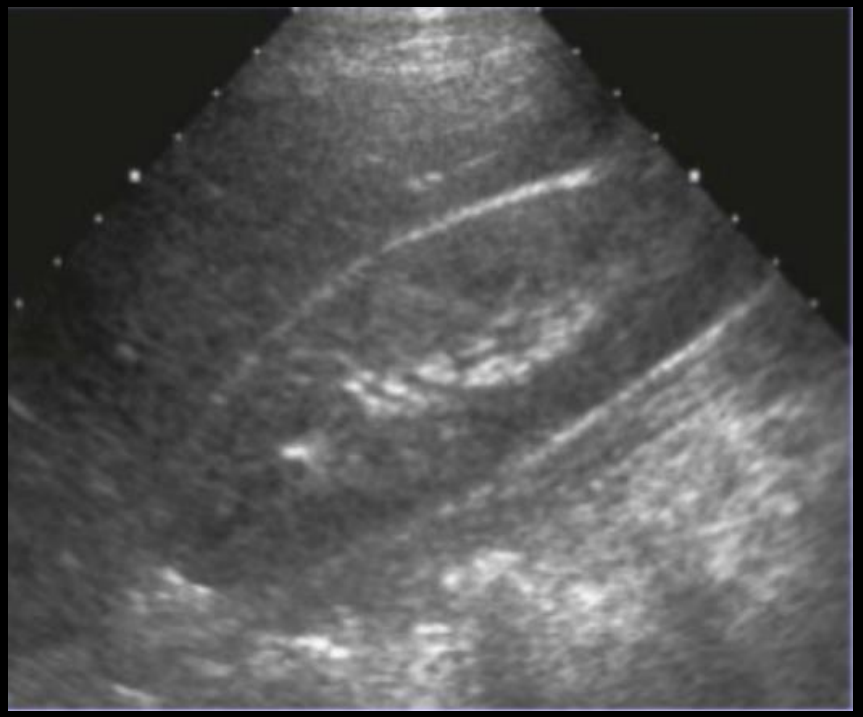
- Ateş: 38.2^{o}C
- Nb: 110/dak, AKB: 110/70 mmHg
- Suprapubik hassasiyet
- Bilateral kostovertebral hassasiyet
- Diğer sistemler tabii

Laboratuar Bulguları

- Beyaz Küre: 12.300 / mm3
- Sedimentasyon: 57 mm/saat
- CRP: 43.8 mgr/L (0-5)
- Tam idrar:
  - Nitrit testi (+)
  - Her sahada 25-30 lökosit ve lökosit kümeleri, 5-6 eritrosit

Radyolojik Bulgular





- Sol böbrek boyutlarında artış
- Parankim ekojenitesinin kaybı
- Kortikomedüller ayrımın yapılamaması

İdrar Kültürü

- *Escherichia coli* > 100.000 cfu/mL

Antibiyotikler	Duyarlı	Dirençli
Ampisilin		+
Amoksilin Klavulonat	+	
Sefuroksim		+
Aztreonam		+
Seftriakson		+
Sefepim	+	
Piperasilin/Tazobaktam	+	
Siprofloksasin		+
TMP/SMX		+
Amikasin	+	
Ertapenem	+	
İmipenem	+	

GSBL (+) *E.coli*

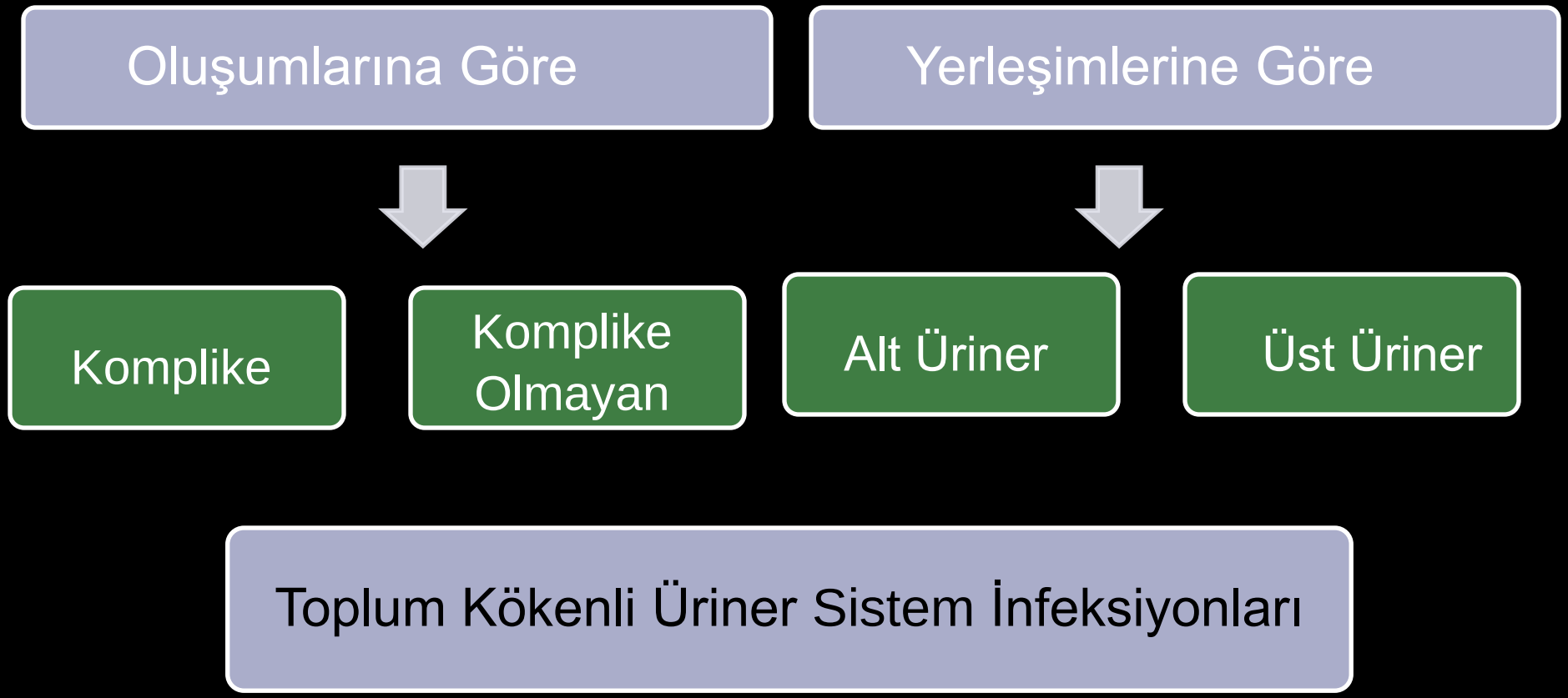
Sorular

- Bu hastalarda tanı nedir?
- İlk tedavi planlaması ne kadar doğrudur?
- Kültür antibiyogram ne zaman yapılmalıdır?
- GSBL pozitifliği bizi nasıl yönlendirmelidir?

Olgu 1 ve 2'de Tedavi

- *Escherichia coli* >100.000 CFU/mL
- GSBL (Pozitif)
- Ertapenem 1x1 gr/gün (7 gün ve 14 gün)
- Tedavinin ilk üç günü içerisinde ateş ve semptomlara yanıt alındı
- Tedavi sonrası idrar kültürü negatif.

Üriner Sistem İnfeksiyonlarında Tanı



Cao J, et al. J Clin Pharmacol 2013

Soru

Olgu 1 ve Olgu 2'nin tanısı?

- **Akut Komplike Olmayan (Basit) Sistit**
- **Akut Komplike Olmayan Piyelonefrit**
- **Nüks (Relaps)**
- **Reinfeksiyon**

- **Olgu 1: AKOS, Nüks**
- **Olgu 2: AKOP, Reinfeksiyon**

İdrar Kültürü Hangi Durumda Alınmalıdır?

- Komplike Üriner Sistem İnfeksiyonları
- Transplantlı hastalarda görülen ÜSİ
- Gebelerde semptomatik olgular
- Gebelerde Asemptomatik Bakterüri taramalarında
- Pediyatrik hastalar, immunsupresifler..
- Tedaviye klinik yanıt alınamaması durumunda
- AKOP
- AKOS
  - Nüks durumlarında
  - Tedaviye yanıtsız olgularda

Soru

Tedavi yaklaşımımız ne olmalıdır?

IDSA ve KLİMİK Uzlaşı Raporu

- TMP/SMX
- Kinolonlar

- Klinik Etkin
- Maliyet Etkin
- İyi tolere edilirl

Fosfomisin
Nitrofrontain..

- Tedavi süresi 3 gü
- TMP/SMX direncini >%20 olması durumunda kinolonlar..

IDSA ve KLİMİK Uzlaşı Raporu

- Nitrofrontain (7 gün)
- Fosfomisin (tek doz)

- Klinik Etkinlik sınırlı
- Maliyet etkin d
- İlk seçenek değ

TMP/SMX ve Kinolon direnci ile önemleri daha da arttı..

- Sistemik bulguların arlığında etkisiz
- Lokal direnç oranları izlenmeli..

Soru

Toplum kökenli GSBL bir sorun olarak değerlendirilmeli mi?

TEDAVİ

İZLEM

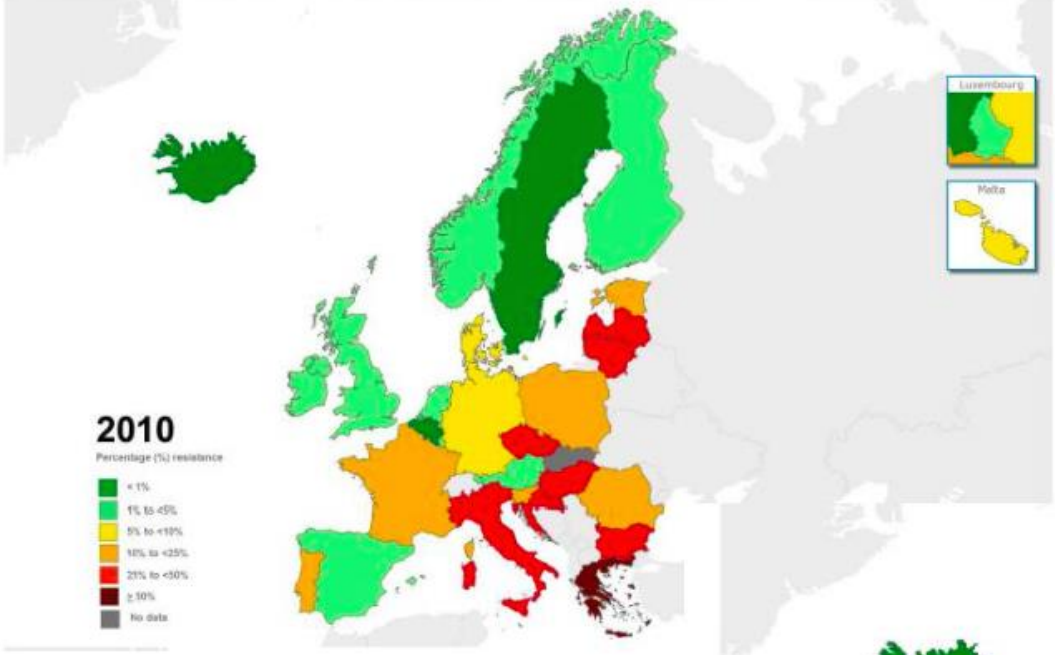
KONTROL

Sentry Antimikrobiyal Sürveyans Verileri

	Escherichia coli	*Klebsiella pneumoniae*
ABD	%13.7 (4-24)	%23 (11-35)
Avrupa	%16.6	%41.8

Sader HS, et al. Diagn Microbiol Infect Dis, 2014

Figure 1. *Klebsiella pneumoniae*: percentage of invasive isolates with combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides, EU/EEA, 2010 (top), 2013 (bottom)

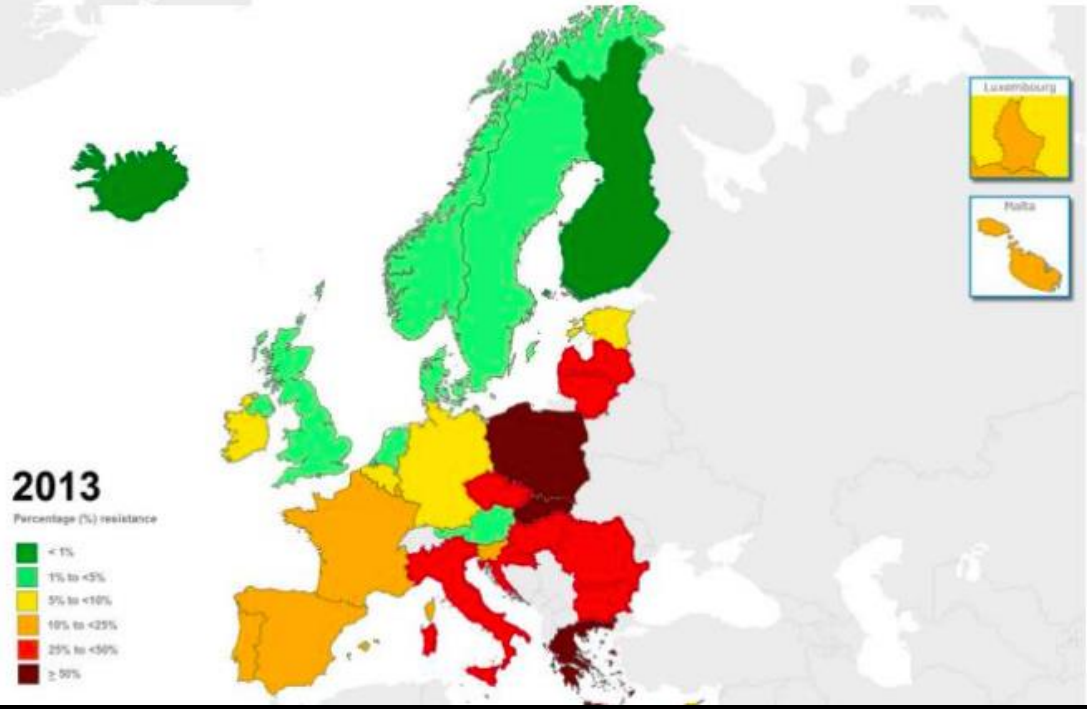


Kinolon, 3. kuşak sefalosporin ve aminoglikozidlere karşı kombine direnç oranı

%10 ➡ %21

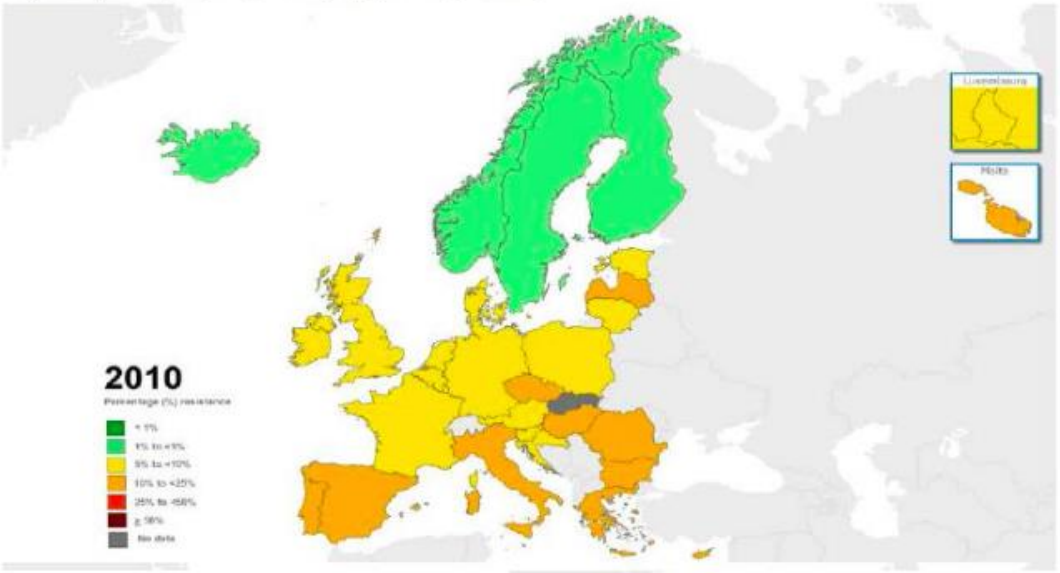
Karbapenem direnci

%4,6 ➡ %8,3



EARS-Net interactive database:
http://www.ecdc.europa.eu/en/healthtopics/antimicrobial-resistance/database

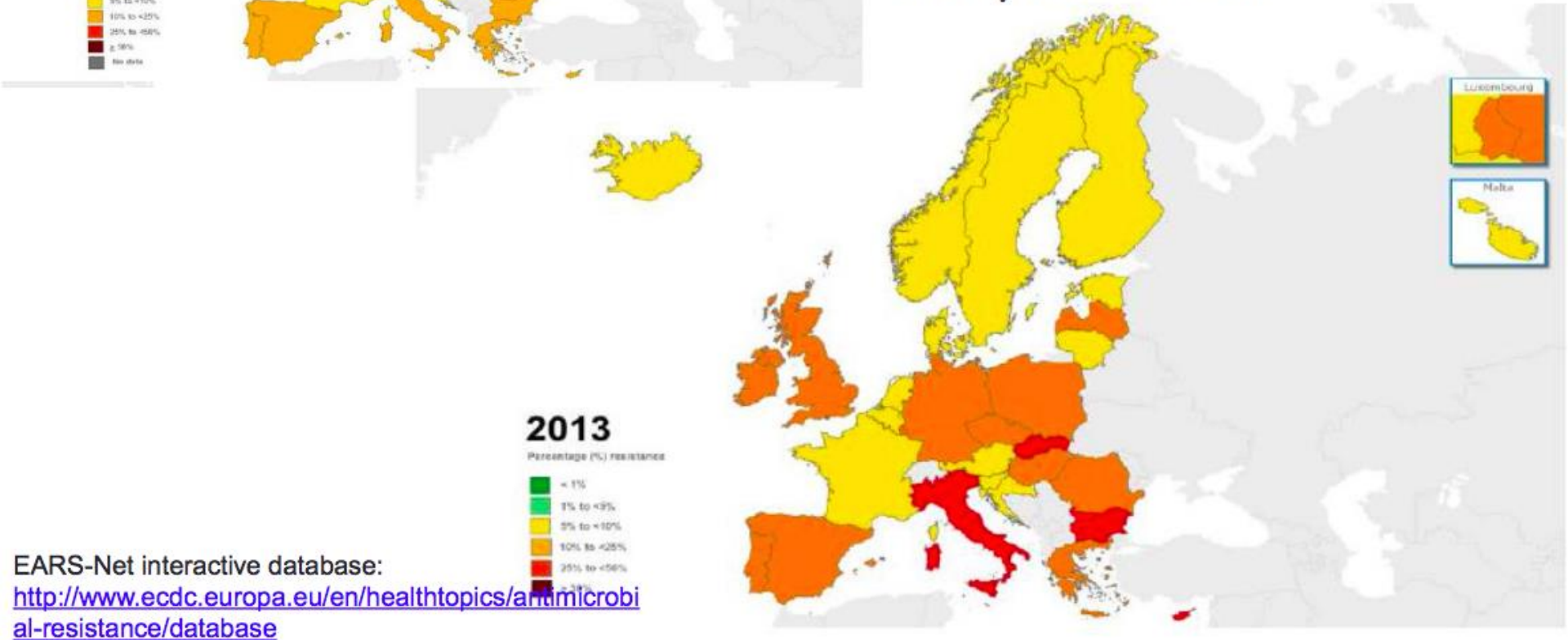
Figure 3. *Escherichia coli*: percentage of invasive isolates with resistance to third-generation cephalosporins, EU/EEA, 2010 (top), 2013 (bottom)



3. kuşak sefalosporine karşı direnç oranı

%9,5 ➡ %12,6

Karbapenem direnci düşük düzeylerde kaldı.



EARS-Net interactive database:
http://www.ecdc.europa.eu/en/healthtopics/antimicrobial-resistance/database

Table A2.4 *Escherichia coli*: Resistance to third-generation cephalosporins[a] European Region

Countries, territories and other areas or groupings	Data source[b,c,d]	Resistance (%)	No. tested isolates	Type of surveillance, population or samples[c]	Period for data collection	Year of publication or report
The former Yugoslav Republic of Macedonia	National data	47.4	19	Invasive isolates		2013
Turkey	National data	43.3	1306	Invasive isolates	2011	2013
Turkmenistan	No information obtained for this report					

Table A2.16 *Klebsiella pneumoniae*: Resistance to third-generation cephalosporins[a] European Region

Countries, territories and other areas or groupings	Data source[b, c, d]	Resistance (%)	No. tested isolates	Type of surveillance, population or samples[c]	Period for data collection	Year of publication or report
Turkey	National data	52.4	794	Invasive isolates	2011	2013
Turkmenistan	No information obtained for this report					
Ukraine	No information obtained for this report[e]					

Toplum Kökenli Üriner Sistem İnfeksiyonları Etkenlerinin Yıllara Göre Dağılımı

Bakteri	AMP	AMC	Sefazolin	Sefuroksim	CRO	CAZ	FEP	SXT	GENTA	CIP	FOSFOM	AK	NITROF	PIPTAZ	IMP	GSBL
E.coli	64	32	40	28	24	11	10	23	18	39	1	1	5	9	1	22
Klebsiella sp.	100	47	100	41	24	25	9	35	17	24	1	18	12	24	1	29
Proteus	35	22		29	5	4	4	42	18	12		5	33	2	3	4
Enterobacter	71	74		43	35	49	12	46	25	15		16	11	21	0	
Serratia	59	65		46	42	54	9	55	18	35	2	10	23	11	0	
Pseudomonas	100	100		100	81	21	17	82	19	62		14	14	9	11	
Enterokok	28		100	100	100			24	13	24		12	12	1		
KNS	33	24	29					15	18	27		18	9			
S.aureus	29	28	28				17	15	20	22		5				
Citrobacter	54	11			34	13	17	25	8	18		11	13	21	1	

Klimik ADÇG Üriner Sistem İnfeksiyonları Uzlaşı Raporu

Journal of Infection (2006) 52, 9–14

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Outpatient prescription of oral antibiotics in a training hospital in Turkey: Trends in the last decade

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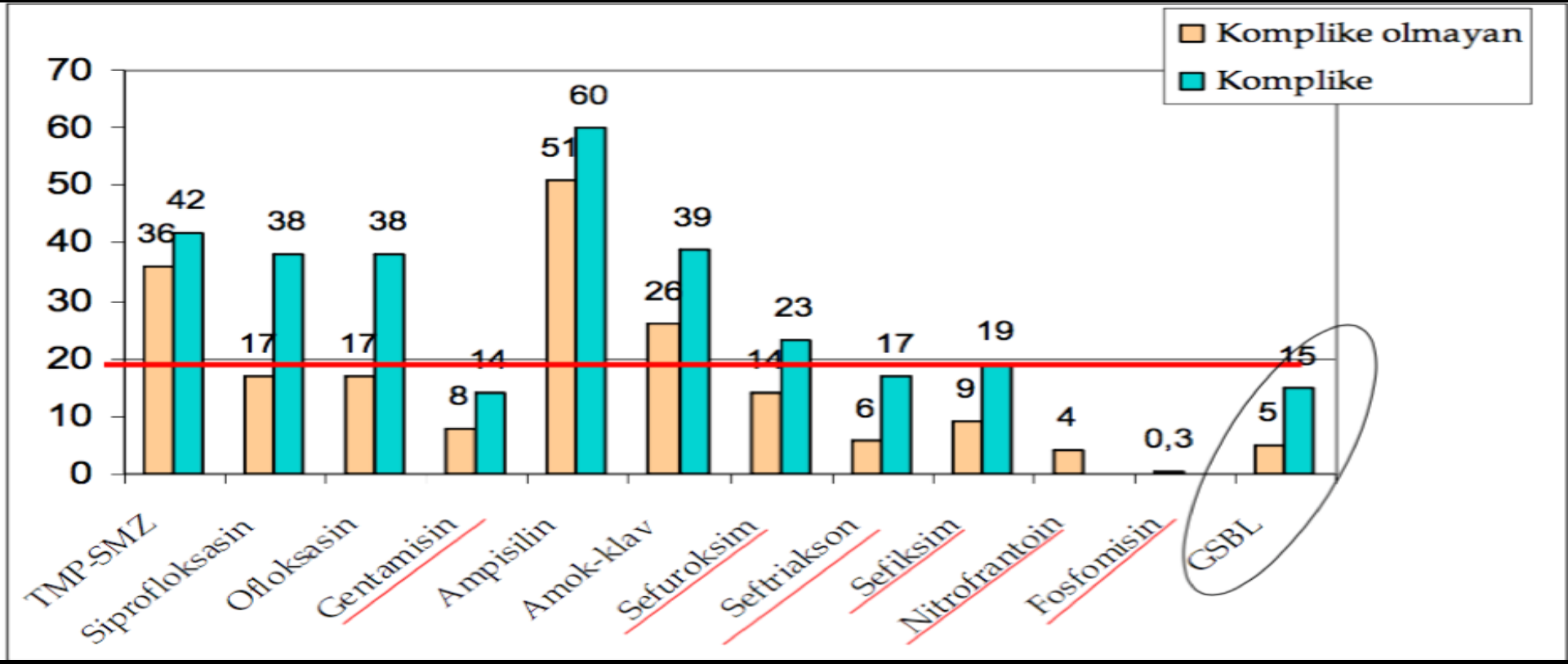
[a]Department of Infectious Diseases and Clinical Microbiology, Gulhane Military Medical Academy,



J Antimicrob Chemother
doi:10.1093/jac/dkw574

Journal of Antimicrobial Chemotherapy

Epidemiology and susceptibility of pathogens from SMART 2011–12 Turkey: evaluation of hospital-acquired versus community-acquired urinary tract infections and ICU- versus non-ICU-associated intra-abdominal infections

Iftihar Koksal[1]*, Gurdal Yilmaz[1], Serhat Unal[2], Pinar Zarakolu[2], Volkan Korten[3], Lutfiye Mulazimoglu[3], Fehmi Tabak[4], Birgul Mete[4], Vildan Avkan Oguz[5], Zeynep Gulay[5], Emine Alp[6], Robert Badal[7] and Sibylle Lob[7]

[1]Karadeniz Technical University, Trabzon, Turkey; [2]Hacettepe University, Ankara, Turkey; [3]Marmara University, Istanbul, Turkey; [4]Istanbul University, Istanbul, Turkey; [5]Dokuz Eylul University, Izmir, Turkey; [6]Erciyes University, Kayseri, Turkey; [7]International Health Management Associates, Inc., Schaumburg, IL, USA

Table 2. ESBL positivity and antibiotic susceptibility rates for *E. coli*, *K. pneumoniae* and all Gram-negative isolates combined in HA versus CA UTIs

	n	ESBL (%)	ETP	IPM	AMK	FEP	CTX	FOX	CAZ	CRO	CIP	LVX	SAM	TZP
E. coli														
HA	109	**50.5***	**97.3**	**100**	**96.3**	54.1	48.6	**96.3**	58.7	49.5	4			6
CA	68	**38.2**	**98.5**	**100**	**97.1**	60.3	58.8	**92.7**	67.7	58.8	6			9
K. pneumoniae														
HA	61	**44.3**	80.3	86.9	**95.1**	60.7	47.5	80.3	62.3	55.7	6			9
CA	12	**41.7**	**100**	**100**	83.3	66.7	58.3	**100**	58.3	58.3	5			0
All Gram-negative														
HA	271		76.4	80.8	**90.0**	60.5	44.6	64.2	62.7	46.1	6			4
CA	92		**96.7**	**96.7**	**95.7**	64.1	57.6	**90.2**	69.6	55.4				0

Toplum Kökenli ÜSİ' larında artan GSBL Aktivitesi

ETP, ertapenem; IPM, imipenem; AMK, amikacin; FEP, cefepime; CTX, cefotaxime; FOX, cefoxitin; CAZ, ceftazidime; CRO, ceftriaxone; CIP, ciprofloxacin; LVX, levofloxacin; SAM, ampicillin/sulbactam; TZP, piperacillin/tazobactam.
Susceptibility of all Gram-negative species combined is shown using breakpoints appropriate for each species (0% susceptible assumed for species with no breakpoints for any given drug). Susceptibility values ≥90% are shown in bold and differences ≥10% between HA and CA isolates are underlined.
*$P < 0.001$ compared with CA UTIs.


madalyonun
öbür yüzü
LİNAMİGUE
aysenurogras
— Madalyonun arka yüzü...
— Madalyonun arka yüzü...
DEVLET KORUMA
Sözler
ANKARA TELVİZYON
GSBL
Direncinin
Ötesi..


EXTENDED SPECTRUM
β-LACTAMASE (ESBL) PRODUCING
ENTEROBACTERIACEAE
26,000
CARBAPENEM-RESISTANT
ENTEROBACTERIACEAE
9,000
600 DEATHS
1,400
7,900
CRE HAVE BECOME RESISTANT TO ALL
OR NEARLY ALL AVAILABLE ANTIBIOTICS
THREAT LEVEL
SERIOUS
THREAT LEVEL
URGENT

GSBL Pozitifliği İçin Risk Faktörleri (Çok Değişkenli Analiz)

	Odds ratio	Güvenlik aralığı	*P* value
Bir yıl içinde > 3ÜSİ atağı	3.5	1.59-7.76	0.002
Son 3 ay içinde B-laktam kullanımı	4.5	1.83-11.18	0.001
Son 2 hafta içinde antibiyotik kullanımı	2.4	1.08-5.35	0.031
Son 2 hafta içinde B-laktam kullanımı	4.9	1.20-20.49	0.026

Recommendation for treatment of severe infections caused by Enterobacteriaceae producing extended-spectrum β-lactamases (ESBLs)

D. L. Paterson

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Extended-spectrum β-lactamase (ESBL)-producing organisms are a global problem. No randomized controlled trials have ever been performed to guide optimal treatment. However, in vitro studies and observational studies strongly suggest that carbapenems (imipenem or meropenem) should be regarded as drugs of choice for serious infections due to ESBL-producing organisms. Other β-lactam antibiotics (cefepime, β-lactam/β-lactamase inhibitor combinations) are not suitable as first-line therapy. The increasing frequency of the association between quinolone resistance and ESBL production have greatly

Table 1 Treatment recommendations for infections caused by organisms producing extended-spectrum β-lactamases (ESBLs)

Type of infection	First-line therapy	Second-line therapy
Bacteremia	Carbapenem[a] (imipenem or meropenem)	Ciprofloxacin
Nosocomial pneumonia	Carbapenem (imipenem or meropenem)	Ciprofloxacin
Intra-abdominal infection	Carbapenem[a] (imipenem or meropenem)	Ciprofloxacin
Urinary tract infection	Ciprofloxacin	Amoxycillin–clavulanate
Meningitis	Meropenem[a]	Addition of polymyxin B

[a]Removal of central venous lines, drainage of collections and removal of neurosurgical hardware is important for optimal outcome of these infections.

Clinical Infectious Diseases Advance Access published January 29, 2

MAJOR

Carbapenem Therapy Is Associated With Improved Survival Compared With Piperacillin-Tazobactam for Patients With Extended-Spectrum β-Lactamase Bacteremia

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Background. The effectiveness of piperacillin-tazobactam (PTZ) for the treatment of extended-spectrum β-lactamase (ESBL) bacteremia is controversial. We compared 14-day mortality of PTZ vs carbapenems as empiric therapy in a cohort of patients with ESBL bacteremia who all received definitive therapy with a carbapenem.

Methods. Patients hospitalized between January 2007 and April 2014 with monomicrobial ESBL bacteremia were included. A decrease of >3 doubling dilutions in the minimum inhibitory concentration for third-generation cephalosporins tested in combination with 4 μg/mL of clavulanic acid was used to confirm ESBL status. The primary exposure was empiric therapy, defined as antibiotic therapy administered to a patient before ESBL status was known. Patients were excluded if they did not receive a carbapenem after ESBL production was identified. The primary outcome was time to death from the first day of bacteremia. Propensity scores using inverse probability of exposure weighting (IPW) were used to estimate the probability that a patient would receive PTZ vs carbapenems empirically. We calculated overall hazard ratios for mortality censored at 14 days using Cox proportional hazards models on an IPW-adjusted cohort.

Results. A total of 331 unique patients with ESBL bacteremia were identified. One hundred three (48%) patients received PTZ empirically and 110 (52%) received carbapenems empirically. The adjusted risk of death was 1.92 times higher for patients receiving empiric PTZ compared with empiric carbapenem therapy (95% confidence interval, 1.07–3.45).

Conclusions. PTZ appears inferior to carbapenems for the treatment of [illegible] risk of invasive ESBL infections, early [illegible]

UPDATE

Recommendation for treatment of severe infections caused Enterobacteriaceae producing extended-spectrum β-lactam

D. L. Paterson

Infectious Disease Section, Instituto per I Trapianti Terapie as Alta Specializzazione, Palermo, Italy and I Division, University of Pittsburgh Medical Center, Pittsburgh, USA

Extended-spectrum β-lactamase (ESBL)-producing organisms are a global problem. No ran controlled trials have ever been performed to guide optimal treatment. However, in vitro stu observational studies strongly suggest that carbapenems (imipenem or meropenem) should b drugs of choice for serious infections due to ESBL-producing organisms. Other β-lactam an (cefepime, β-lactam/β-lactamase inhibitor combinations) are not suitable as first-line therap increasing frequency of the association between quinolone resistance and ESBL production l limited the role of this class of antibiotic against ESBL producers.

Keywords ESBL, extended-spectrum beta-lactamase, beta-lactamase, carbapenems, cepha *Klebsiella*

Accepted 17 May 2000

Clin Microbiol Infect 2000; 6: 460–463

Cefepime Therapy for Monomicrobial Bacteremia Caused by Cefepime-Susceptible Extended-Spectrum Beta-Lactamase–Producing *Enterobacteriaceae*: MIC Matters

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DOI: 10.1093/cid/cis916

Nan-Yao Lee,[1,2] Ching-Chi Lee,[1,2] Wei-Han Huang,[4] Ko-Chung Tsui,[5,8] Po-Ren Hsueh,[6,7,a] and Wen-Chien Ko[1,2,3,a]

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Background. Extended-spectrum ß-lactamase (ESBL)–producing *Enterobacteriaceae* isolates are important clinical pathogens. In addition, the efficacy of cefepime for such infections is controversial.

Methods. We performed a retrospective study of monomicrobial bacteremia caused by ESBL producers at 2 medical centers between May 2002 and August 2007. The patients definitively treated with in vitro active cefepime (cases) were compared with those treated with a carbapenem (controls) in a propensity score–matched analysis to assess therapeutic effectiveness. The 30-day crude mortality is the primary endpoint.

Results. A total of 178 patients were eligible for the study. Patients who received cefepime (n = 17) as definitive therapy were more likely to have a clinical failure (odds ratio [OR] 6.2; 95% confidence interval [CI], 1.7–22.5; $P = .002$), microbiological failure (OR 5.5; 95% CI, 1.3–25.6; $P = .04$), and 30-day mortality (OR 7.1; 95% CI, 2.5–20.3; $P < .001$) than those who received carbapenem therapy (n = 161). Multivariate regression revealed that a critical illness with a Pitt bacteremia score ≥4 points (OR 5.4; 95% CI, 1.4–20.9; $P = .016$), a rapidly fatal underlying disease (OR 4.4; 95% CI, 1.5–12.6; $P = .006$), and definitive cefepime therapy (OR 9.9; 95% CI, 2.8–31.9; [illegible] independently associated with 30-day crude mortality. There were 17 case-control pairs in the [illegible] analysis consistently found that individuals who received cefe-

Bacteremia Due to *Klebsiella pneumoniae* Isolates Producing the TEM-52 Extended-Spectrum β-Lactamase: Treatment Outcome of Patients Receiving Imipenem or Ciprofloxacin

Andrea Endimiani,[1] Francesco Luzzaro,[1] Mariagrazia Perilli,[2] Gianluigi Lombardi,[1] Alessandra Coli,[1] Antonio Tamborini,[1] Gianfranco Amicosante,[2] and Antonio Toniolo[1]

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The treatment outcome of 35 cases of bacteremia due to *Klebsiella pneumoniae* isolates producing TEM-52 extended-spectrum β-lactamase was studied. Twenty-eight cases, classified as "nonfatal disease" using the McCabe and Jackson classification, were investigated with regard to ciprofloxacin and imipenem response. Because ciprofloxacin was active in vitro against 21 of 28 isolates, only the treatment outcome of the ciprofloxacin-susceptible subgroup was evaluated. Eight of 10 cases occurred in patients who experienced a complete response to imipenem; 2 of 10 failed to respond. In contrast, only 2 of 7 cases had a partial response to ciprofloxacin, and, in 5 of 7 cases, the treatment failed. Statistical analysis revealed a significant difference in the treatment outcome of the 2 groups ($P = .03$). Because the isolates had minimum inhibitory concentrations of ciprofloxacin close to the susceptibility breakpoint, treatment failure could be ascribed to the inability of the drug to reach therapeutic concentrations at infected sites.

Clinical Infectious Diseases 2004; 38:243–51

1058-4838/2004/3802-0009$15.00

GSBL (+) Enterobacteriaceae Tedavisinde Güvenilir İlaçlar

- Karbapenemler (Kanıtlanmış etkinlik..)
- Fosfomisin
- Piperasilin/Tazobaktam (İnokulum etkisi)
- Sefepim (İnokulum etkisi)
- Amikasin
- Tigesiklin (P.mirabilis hariç)
- Kinolonlar

Pitout JD. Lancet ID 2008

GSBL Tedavisi

- GSBL infeksiyon tedavisi sorunlu
- Tedavi seçenekleri sınırlı
- Prognoz GSBL (-) olanlara göre daha kötü
- GSBL (+) ÜSİ'larında
  - Karbapenemler
  - PIP/TAZ
  - Sefepim
  - Kinolonlar etkilidir.
- Ancak bakteremide MİK düzeyleri önemli..

Antibiyotik	**Eski M100-S19 (2009)** MİK değerleri mg/L			**Yeni M100-S20 (2010)** MİK değerleri mg/L		
	Duyarlı (S)	I	Dirençli (R)	Duyarlı (S)	I	Dirençli (R)
Sefazolin	**≤8**	16	≥32	**≤1**	2	≥4
Sefotaksim	**≤8**	16-32	≥64	**≤1**	2	≥4
Seftizoksim	**≤8**	16-32	≥64	**≤1**	2	≥4
Seftriakson	**≤8**	16-32	≥64	**≤1**	2	≥4
Seftazidim	**≤8**	16	≥32	**≤4**	8	≥16
Aztreonam	**≤8**	16	≥32	**≤4**	8	≥16

Antibiyotik	Eski M100-S19 (2009) Disk difüzyon zon çapları (mm)			**Yeni M100-S20 (2010)) Disk difüzyon zon çapları (mm)**		
	Duyarlı (S)	I	Dirençli (R)	Duyarlı (S)	I	Dirençli (R)
Sefazolin	≥ 18	15-17	≤14	-	-	-
Sefotaksim	≥23	15-22	≤14	≥ 26	23-25	≤ 22
Seftizoksim	≥20	15-19	≤14	≥25	22-24	≤21
Seftriakson	≥ 21	14-20	≤13	≥23	20-22	≤19
Seftazidim	≥18	15-17	≤14	≥21	18-20	≤17
Aztreonam	≥22	16-21	≤15	≥21	18-20	≤17

GSBL (+) Üst ÜSİ'larında Takip

- Karbapenem dışı tedaviler söz konusu ise
- Bakteremi gelişimiyle tedavi yanıtı olumsuz..
- Mortalite ve morbidite artışı.

J Clin Pharmacol 2013

JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Developing a model to estimate the probability of bacteremia in women with community-onset febrile urinary tract infection

Won Sup Oh[1], Yeon-Sook Kim[2], Joon Sup Yeom[3], Hee Kyoung Choi[4,5], Yee Gyung Kwak[6], Jae-Bum Jun[7], Seong Yeon Park[8], Jin-Won Chung[9], Ji-Young Rhee[10], Baek-Nam Kim[11]

Table 2. Predictors associated with bacteremia in women with community-onset febrile urinary tract infection.

Predictors	β coefficients	OR (95% CI)	p value	Points
Diabetes mellitus	0.682	1.959 (1.092–3.514)	0.024	1
Urinary tract obstruction by stone	1.061	2.888 (1.154–7.228)	0.023	2
Tenderness on costovertebral angle	1.168	3.216 (1.687–6.130)	< 0.001	2
Fraction of segmented neutrophils > 90%	1.306	3.691 (2.010–6.777)	< 0.001	2
Platelet < 150,000/μL	1.204	3.333 (1.831–6.068)	< 0.001	2
BUN > 20 mg/dL or creatinine > 1.5 mg/dL	1.116	3.052 (1.708–5.455)	< 0.001	2
Fulfillment of all SIRS criteria [a]	1.205	3.336 (1.440–7.729)	0.005	2

BUN: blood urea nitrogen; CI: confidence interval; OR: odds ratio; SIRS: systemic inflammatory response syndrome; [a] Including (1) heart rate > 90 beats/min, (2) respiratory rate > 20 breaths/min, (3) temperature > 38°C or < 36°C, or (4) white blood cell > 12,000/μL, < 4,000/μL, or band form > 10%.

Table 3. Risk stratification for bacteremia according to the model score.

Risk stratification for bacteremia (predicted probability)	Model score	No. of bacteremia /total
Low (< 10%)	0–2	16/163 (9.8%)
Intermediate (10–30%)	3–5	41/140 (29.3%)
High (> 30%)	≥ 6	58/80 (72.5%)
Total		**115/383 (30.0%)**

ARTICLE IN PRESS

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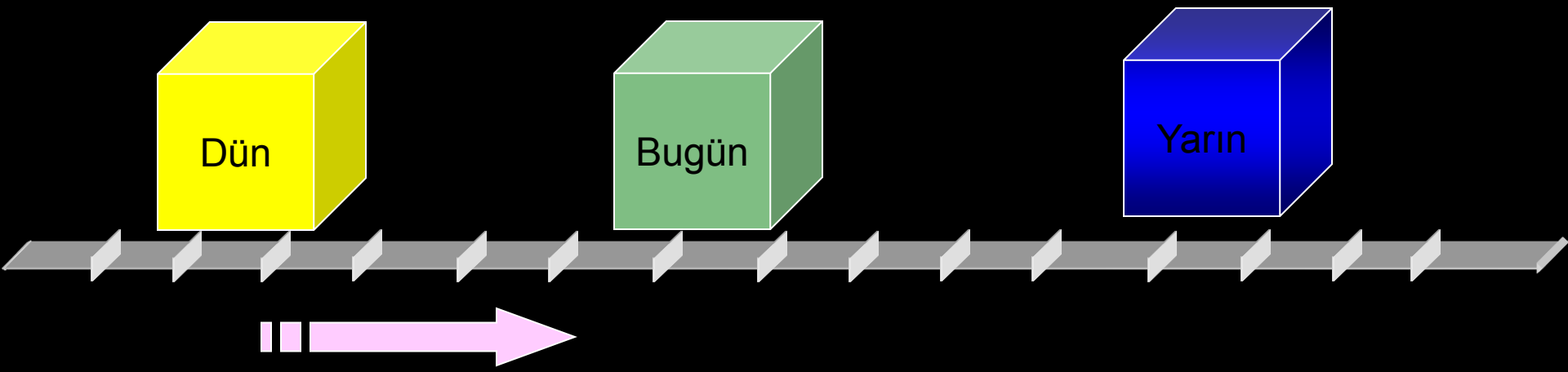
Yeni antimikrobiyaller

- Sefepim-sulbaktam
- Seftriakson-sulbaktam
- Seftazidim-avibaktam (komplike karın içi ve üriner sistem infeksiyonları)
- Seftolozan-tazobaktam (komplike karın içi ve üriner sistem infeksiyonları)
- Seftarolin-avibaktam
- Tigesiklin (komplike karın içi ve deri ve yumuşak doku infeksiyonları)

Toplum Kaynaklı GSBL Oranlarının İzleminde Hedefler



Artan GSBL Direnci en ciddi sorun..

Bu durum Karbapenem direnci için potansiyel risk..

ÖNLEYİCİ YAKLAŞIM TEDAVİDEN DAHA ÖNCELİKLİ..

Open Forum Infectious Diseases

MAJOR ARTICLE

Carbapenem-Resistant *Klebsiella pneumoniae* Infection in Three New York City Hospitals Trended Downwards From 2006 to 2014

Sun O. Park,[1,4] Jianfang Liu,[2] E. Yoko Furuya,[3] and Elaine L. Larson[1,2]

[1]Mailman School of Public Health, [2]School of Nursing, and [3]College of Physicians and Surgeons, Columbia University, New York; [4]Department of Medicine, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, New York

Background. Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) infection is a rising public health threat since its first outbreaks in New York City (NYC) in the early 2000s. We investigated annual trends of CRKP infection in hospital-acquired infections (HAIs) and community-onset infections (COIs) treated in 3 NYC hospitals from 2006 to 2014.

Methods. We extracted *K pneumoniae* infection data including carbapenem susceptibility and anatomical sites, compared clinical characteristics between CRKP and carbapenem-susceptible *K pneumoniae* infections, and determined CRKP infection proportions in total *K pneumoniae* infections in HAI and COI to identify statistically significant trends from 2006 to 2014 using the Cochran-Armitage trend test.

Results. Carbapenem-resistant *K pneumoniae* contributed 17.3% (601 of 3477) of hospital-acquired *K pneumoniae* infection compared with 7.7% (149 of 1926) in COI from 2006 to 2014. Carbapenem-resistant *K pneumoniae* proportions in HAI and COI were positively correlated over time ($r = 0.83$, $P < .01$), and there were downward annual trends of CRKP proportions from 2006 to 2014 in both HAI and COI (25.8% to 10.5% in HAI, $P < .001$; 13.6% to 3.1% in COI, $P < .001$). By anatomical site, significant downward annual trends were present only in urinary tract infection ($P < .001$ for both HAI and COI) from 2006 to 2014.

Conclusions. Annual trends of CRKP proportions from 2006 to 2014 were downward in both HAI and COI, and HAI and COI were positively correlated. Efforts to reduce and prevent CRKP infections in both hospital and community settings were successful and warrant continuation.

Keywords. carbapenem-resistant *Klebsiella pneumoniae* (CRKP); carbapenem-susceptible *Klebsiella pneumoniae* (CSKP); community-onset infection (COI); hospital-acquired infection (HAI).

Table 1. Clinical Characteristics of Patients With Carbapenem-Resistant vs Carbapenem-Susceptible *Klebsiella pneumonia* in Hospital-Acquired and Community-Onset Infections

	Hospital-Acquired Infection (n = 3477)			Community-Onset Infection (n = 1926)		
Characteristics	CRKP (n = 601)	CSKP (n = 2876)	*P* Value	CRKP (n = 149)	CSKP (n = 1777)	*P* Value
Age (year), mean ± SD	62.3 ± 20.0	61.6 ± 24.1	.24	68.5 ± 17.7	65.2 ± 22.4	0.31
Female sex	330 (54.9)	1639 (57.0)	.35	79 (53.0)	1220 (68.7)	<.001
Hospital			<.001[a]			.09[a]
1 (tertiary)	466 (77.5)	2134 (74.2)		106 (71.1)	1234 (69.4)	
2 (community)	112 (18.6)	430 (15.0)		40 (26.9)	429 (24.1)	
3 (children's)	23 (3.8)	312 (10.8)		3 (2.0)	114 (6.4)	
Anatomical site			<.001[a]			
UTI	372 (61.9)	1807 (62.8)				
PNU						
BSI						
Diab						
Mali						
Dialy						
Histc						
Charl						
Prior						
Hospi						
ICU st						
ICU da						
Antibic					N/K	N/K

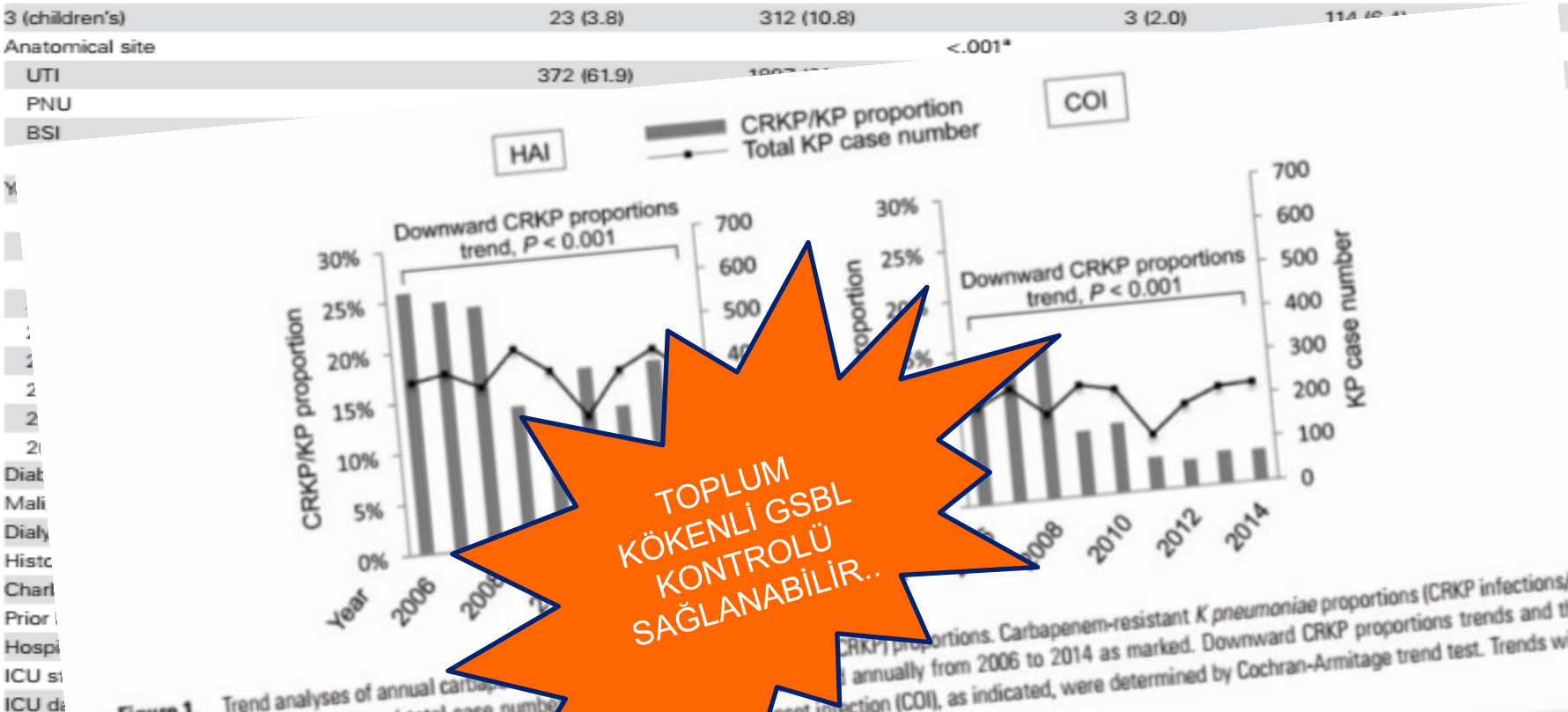


Figure 1. Trend analyses of annual carba… *pneumoniae* [KP] infections) and total case numbe… corresponding *P* values in hospital-acquired infe… *P* < .05 are considered statistically significant.

…portions. Carbapenem-resistant *K pneumoniae* proportions (CRKP infections/*K* … annually from 2006 to 2014 as marked. Downward CRKP proportions trends and the …nset infection (COI), as indicated, were determined by Cochran-Armitage trend test. Trends with

TOPLUM KÖKENLİ GSBL KONTROLÜ SAĞLANABİLİR..

Abbrevi… …usceptible *K pneumoniae*; ICU, intensive care unit; LOS, length of stay; N/A, not applicab…

Note: Da… …site infection; UTI, urinary tract infection.

…were obtained from bivari… analyses.

[a]Overall … for a variable with multiple categories.

[b]Prior hospitalization at the study in New York City hospitals.

[c]Longer than 1 day of any oral or parenteral antibiotic use including β-lactams, β-lactam-β-lactamase inhibitor, fluoroquinolones, and aminoglycosides.

PLOS ONE

RESEARCH ARTICLE

Fecal carriage of extended spectrum β-lactamase producing *Escherichia coli* and *Klebsiella pneumoniae* after urinary tract infection – A three year prospective cohort study

Silje B. Jørgensen[1,2]*, Arne Søraas[1,3], Arnfinn Sundsfjord[4,5], Knut Liestøl[6], Truls M. Leegaard[2,7], Pål A. Jenum[1,7]

1 Department of Laboratory Medicine, Section for Medical Microbiology, Vestre Viken Hospital Trust, Bærum, Norway, **2** Department of Clinical Microbiology and Infection Control, Akershus University Hospital, Lørenskog, Norway, **3** Department of Infectious Diseases, Oslo University Hospital, Oslo, Norway,

Table 2. Multiple logistic regression model of potential risk factors for ESBL-E carriage 13 months after urinary tract infection.

			Univariate analysis			Multivariate analysis		
Variable	**ESBL-positive (n = 44)**	**ESBL-negative (n = 39)**	**OR**	**95% CI**	**P**	**OR**	**95% CI**	**P**
Age > 65 years	18	13	1.4	0.59–3.5	0.426	1.8	0.60–5.4	0.294
Male sex	5	5	0.9	0.24–3.4	0.872	0.85	0.18–3.9	0.833
Chronic urinary tract infection	11	9	1.2	0.42–3.2	0.788	1.0	0.32–3.3	0.957
Charlson score[29] >2	7	4	1.7	0.46–6.3	0.426	1.7	0.39–7.2	0.480
Number of household members >3	8	5	1.6	0.46–5.2	0.474	1.5	0.37–5.8	0.594
***E. coli* phylogroup B2 or D in urine**	37	24	3.3	1.2–9.3	0.023	3.8	1.2–12.6	0.027
CTX-M group 1 in urine isolate	26	28	0.62	0.25–1.5	0.299	0.70	0.26–1.9	0.492
Antibiotics*	32	31	0.77	0.27–2.1	0.614	0.97	0.32–3.0	0.958
Travel to Asia, Africa or Middle-East	10	10	0.92	0.32–2.4	0.807	0.778	0.25–2.4	0.661

Clearance is defined as two consecutive negative samples. OR = odds ratio for ESBL persistence, CI = confidence interval.

* Any antibiotic received between 14 days and 13 months after positive urinary sample.

Toplum Kökenli GSBL Kontrolü

- Hayvan yemlerindeki antibiyotik katkısının %90'dan %40'lara düşürülmesi..
- Ciddi takip ve yaptırımlar
- Fekal taşıyıcılık oranları ve GSBL ilişkisinin takibi
- Ciddi infeksiyon tablolarında MİK kontrolü ile antibiyotik kullanımı
- Koruyucu tedaviler..

Sonuç

- Toplum kökenli ÜSİ'larının tedavisinde GSBL şüphesi en az 1/3-1/4
- Hastaların takibi önemli
- Rekürrens ve reinfeksiyon sorgulaması
- GSBL yönünden risk faktörlerinin araştırılması
- Üst ÜSİ'larında bakteremi şüphesi
- Fekal taşıyıcılık ve hayvan yemlerinin kontrolü..
- Yeni antibiyotikler ve karbapenemlerin rasyonel kullanımı

Tesekkurler…