Kolistine Dirençli Acinetobacter İnfeksiyonu

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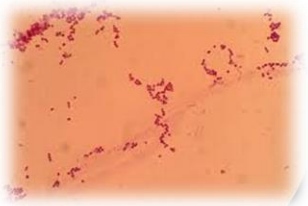

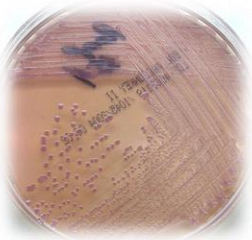

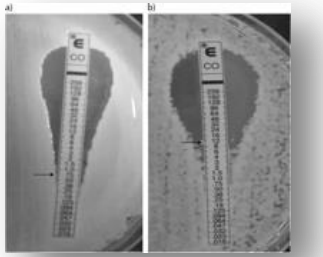

- 1986→ Acinetobacter baumannii taksonomik olarak sınıflandırıldı

Üç ana gruba ayrıldı

- i) **Acinetobacter calcoaceticus-baumannii kompleks**
- → *A. baumannii*, *A. pittii*, *A.nosocomialis* : En sık
- → glukoz oksidasyonu (+), non-hemolitik
- ii) Acinetobacter lwoffii→ glukoz (-), non-hemolitik
- iii) Acinetobacter haemolyticus →hemolitik

Bouvet et al., 1986
Euzeby, 2008

Tam sınıflandırma

Domain	*Bacteria*
Phylum	*Proteobacteria*
Class	*Gammaproteobacteria*
Order	*Pseudomonadales*
Family	*Moraxellaceae*
Genus	*Acinetobacter*
Species	*A. baumannii* *A. baylyi* *A. beijerinckii* *A. bouvetii* *A. calcoaceticus* *A. gerneri* *A. grimontii* *A. gyllenbergii* *A. haemolyticus* *A. johnsonnii* *A. junnii* *A. lwoffii* *A. parvus* *A. radioresistens* *A. schindleri* *A. soli* *A. tandoii* *A. tjernbergiae* *A. towneri* *A. ursingii* *A. venetianus* 14 species are still unnamed

21

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Table 1. Nomenclature of *Acinetobacter baumannii* (Euzeby, 2008)

Acinetobacter türleri

- Hastane çevresel yüzeylerde kolonizasyon
- Cansız yüzeylerde aylarca canlı
- Kuruluğa dirençli
- Alet ilişkili enfeksiyonların en sık nedenlerinden
- Fırsatçı patojen
- **Biyofilm** → fiziksel ve kimyasal dezenfeksiyona direnç

Getchell-White et al., 1989; Jawad et al., 1996

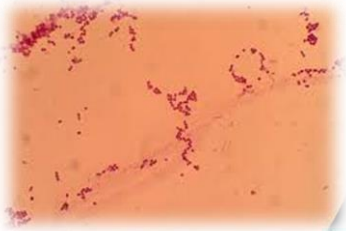
Kramer et al., 2006

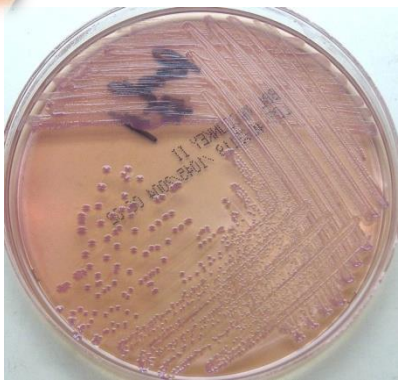
Dima et al., 2007; Thongpiyapoom et al., 2004

Cappelli et al., 2003; Loukili et al., 2006; Pajkos et al., 2004

Acinetobacter baumannii

- Gramda kokobasil görünümü
- MacConkey agarda(soluk pembe renkli koloniler) iyi ürer
- Oksidaz negatif
- **42°C de ürer**
- **OF glukoz ++**
-
-
-
-
-
-
-





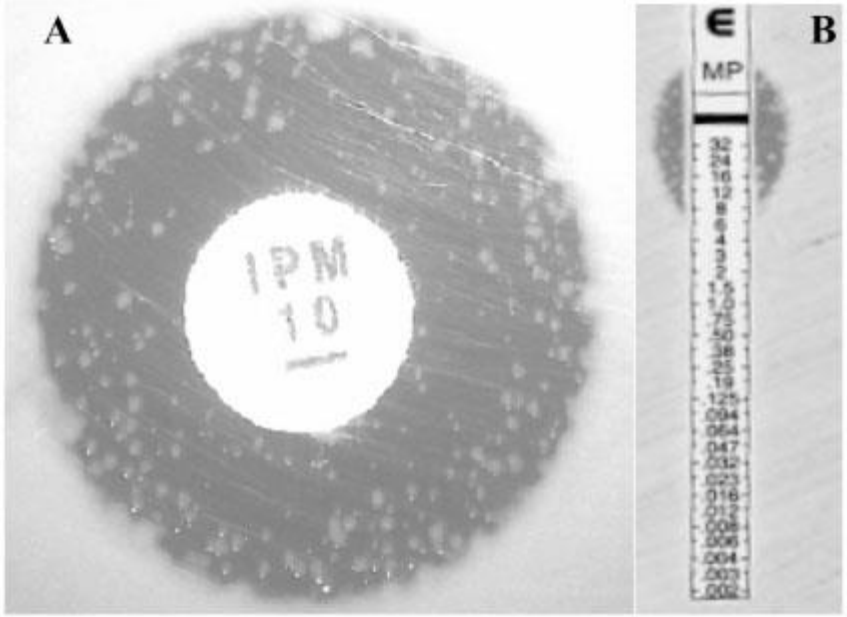
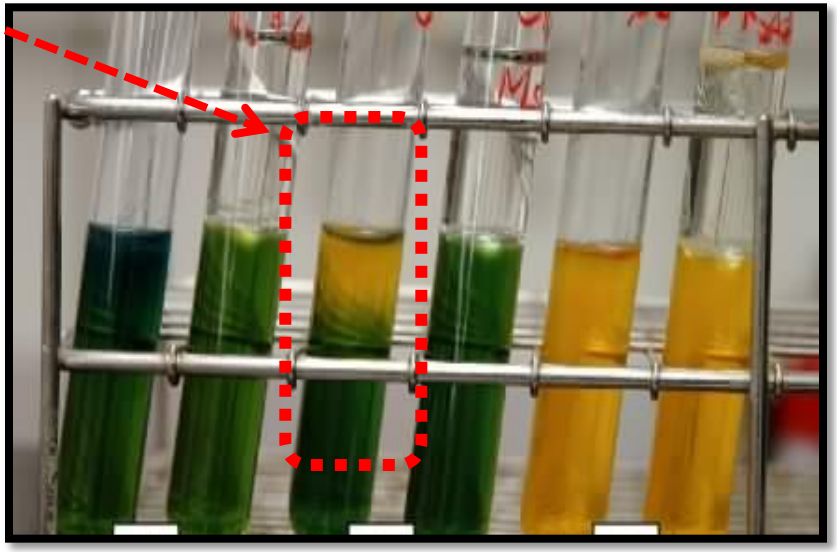
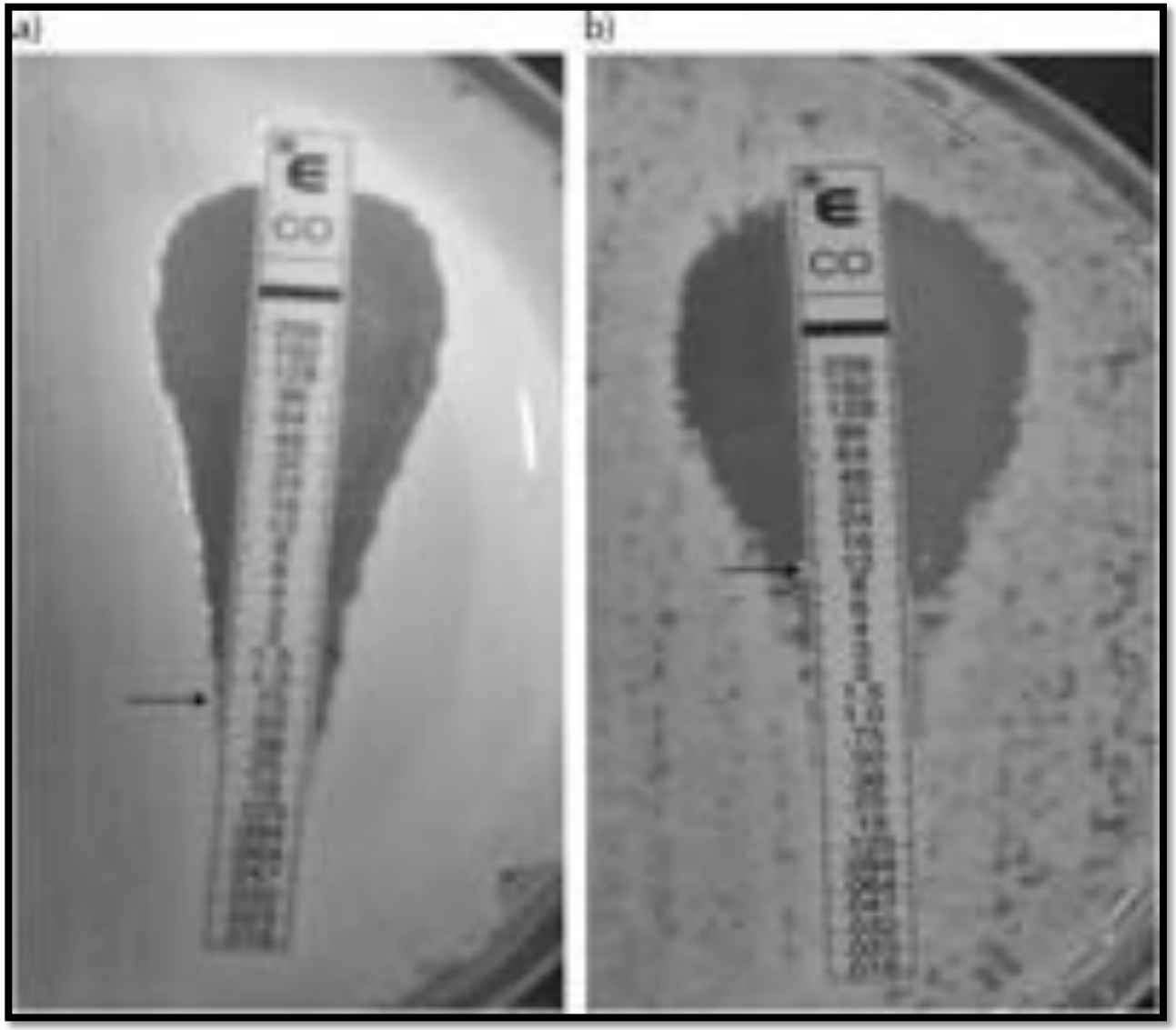


Fig. 1 - Disk-diffusion (A) for imipenem and Etest (B) for meropenem showing the growth of resistant sub-populations of *Acinetobacter baumannii*.




a)
b)

ANTİMİKROBİYAL DİRENÇ ORANLARI

Tablo 20 . Antimikrobiyal Direnç Oranları* ve Dağılımları,2014.

	Antimikrobiyal Direnç Hızları				PERSENTİL				
ANTİMİKROBİYAL DİRENÇLİ PATOJEN	Birim sayısı	Etken sayısı (toplam)	Dirençli etken sayısı	Ağırlıklı genel ortalama	10%	25%	50% (Ortanca)	75%	90%
TÜRKİYE GENELİ									
VRE	607(81)	1798	371	20.63	0.00	0.00	14.29	33.33	50.00
MRSA	400(73)	1731	840	48.53	14.49	28.29	51.85	70.54	85.66
MRKNS	301(86)	2429	2141	88.14	63.94	80.00	90.91	97.81	100.00
E.Coli suşlarında ESBL	457(126)	4688	2755	58.77	34.32	50.00	61.90	80.00	90.20
Klebsiella Pneumoniae suşlarında ESBL	351(114)	3875	2436	62.86	29.66	50.00	69.23	81.56	93.54
Karbapenem dirençli *Acinetobacter baumannii*	338(146)	7197	6589	91.55	80.00	89.72	94.31	98.01	100.00
Karbapenem dirençli *Pseudomonas aeruginosa*	425(113)	3468	1491	42.99	17.75	30.38	41.67	56.31	70.00
Kolistin dirençli *Acinetobacter baumannii*	603(174)	7714	428	5.55	0.00	0.00	2.24	5.88	12.33
SAĞLIK BAKANLIĞI DEVLET HASTANELERİ									
VRE	216(7)	90	7	7.78	–	–	–	–	–
MRSA	155(11)	220	144	65.45	–	–	–	–	–
MRKNS	127(16)	241	208	86.31	–	–	–	–	–
E.Coli suşlarında ESBL	187(43)	989	646	65.32	38.66	50	67.24	81.25	91.15
Klebsiella Pneumoniae suşlarında ESBL	133(33)	571	418	73.20	45.00	60.36	75.00	91.83	98.79
Karbapenem dirençli *Acinetobacter baumannii*	135(52)	1333	1222	91.67	80.55	89.97	94.44	100.00	100.00
Karbapenem dirençli *Pseudomonas aeruginosa*	169(36)	587	250	42.59	10.51	20.43	40.00	57.21	78.59
Kolistin dirençli *Acinetobacter baumannii*	233(58)	1400	54	3.86	0.00	0.00	0.00	6.20	10.18

http://hizmetstandartlari.saglik.gov.tr/dosya/1-97086/h/2014-ulusal-ozet-rapor-1.pdf

ÜNİVERSİTE HASTANELERİ									
VRE	126(42)	1053	254	24.12	0.00	5,22	23,66	39,98	51,40
MRSA	52(24)	765	330	43.14	13.88	21.93	48.19	70.56	79.37
MRKNS	51(31)	1140	1026	90.00	72.77	82.35	90.9	95.00	99.82
E.Coli suşlarında ESBL	57(35)	1984	1126	56.75	41.39	51.35	60.00	74.51	90.00
***Klebsiella Pneumoniae* suşlarında ESBL**	57(34)	1767	1133	64.12	29.66	47.47	65.41	75.11	91.55
Karbapenem dirençli *Acinetobacter baumannii*	50(36)	2921	2650	90.72	79.21	89.66	93.66	97.29	98.76
Karbapenem dirençli *Pseudomonas aeruginosa*	58(34)	1597	663	41.52	18.34	30.12	39.23	55.47	61.85
Kolistin dirençli *Acinetobacter baumannii*	99(44)	3064	166	5.42	0.00	1.40	3.31	5.06	16.27
ÖZEL HASTANELERİ									
VRE	126(5)	71	25	35.21	–	–	–	–	–
MRSA	134(7)	127	76	59.84	–	–	–	–	–
MRKNS	68(9)	127	81	63.78	–	–	–	–	–
E.Coli suşlarında ESBL	152(13)	246	133	54.07	–	–	–	–	–
***Klebsiella Pneumoniae* suşlarında ESBL**	102(11)	226	172	76.11	–	–	–	–	–
Karbapenem dirençli *Acinetobacter baumannii*	92(16)	368	298	80.98	–	–	–	–	–
Karbapenem dirençli *Pseudomonas aeruginosa*	135(5)	88	42	47.73	–	–	–	–	–
Kolistin dirençli *Acinetobacter baumannii*	165(22)	502	127	25.30	0.00	0.00	0.00	48.98	96.66

† Direnç yüzdesi ve persentil dağlımı (parantez içi) birim sayısı. Persentil dağılımında analizlere etken sayısı 10 ve üzerinde olanlar dahil edilmiştir.
MRSA. Metisilin dirençli *Staphylococcus aureus;* VRE. Vankomisin dirençli enterokoklar. ESBL geniş spektrumlu beta laktamaz
Dirençli izolatlar / Test edilen izolat sayısı X 100

http://hizmetstandartlari.saglik.gov.tr/dosya/1-97086/h/2014-ulusal-ozet-rapor-1.pdf

Acinetobacter spp.

EUCAST Clinical Breakpoint Table v. 5.0, valid from 2015-01-01

Macrolides, lincosamides and streptogramins	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes Numbers for comments on MIC breakpoints Letters for comments on disk diffusion
	S ≤	R >		S ≥	R <	
Azithromycin	-	-		-	-	
Clarithromycin	-	-		-	-	
Erythromycin	-	-		-	-	
Roxithromycin	-	-		-	-	
Telithromycin	-	-		-	-	
Clindamycin	-	-		-	-	
Quinupristin-dalfopristin	-	-		-	-	

Tetracyclines	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes Numbers for comments on MIC breakpoints Letters for comments on disk diffusion
	S ≤	R >		S ≥	R <	
Doxycycline	-	-		-	-	
Minocycline	IE	IE		IE	IE	
Tetracycline	-	-		-	-	
Tigecycline	IE	IE		IE	IE	

Miscellaneous agents	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes Numbers for comments on MIC breakpoints Letters for comments on disk diffusion
	S ≤	R >		S ≥	R <	
Chloramphenicol	-	-		-	-	1. Trimethoprim:sulfamethoxazole in the ratio 1:19. Breakpoints are expressed as the trimethoprim concentration.
Colistin	2	2		Note[A]	Note[A]	A. Use an MIC method.
Daptomycin	-	-		-	-	
Fosfomycin iv	-	-		-	-	
Fosfomycin oral	-	-		-	-	
Fusidic acid	-	-		-	-	
Linezolid	-	-		-	-	
Metronidazole	-	-		-	-	
Mupirocin	-	-		-	-	
Nitrofurantoin (uncomplicated UTI only)	-	-		-	-	
Rifampicin	-	-		-	-	
Spectinomycin	-	-		-	-	
Trimethoprim (uncomplicated UTI only)	-	-		-	-	

MİK ≤ 2 µg/mL → DUYARLI

MİK>2 µg/mL → DİRENÇLİ

CLSI 2012

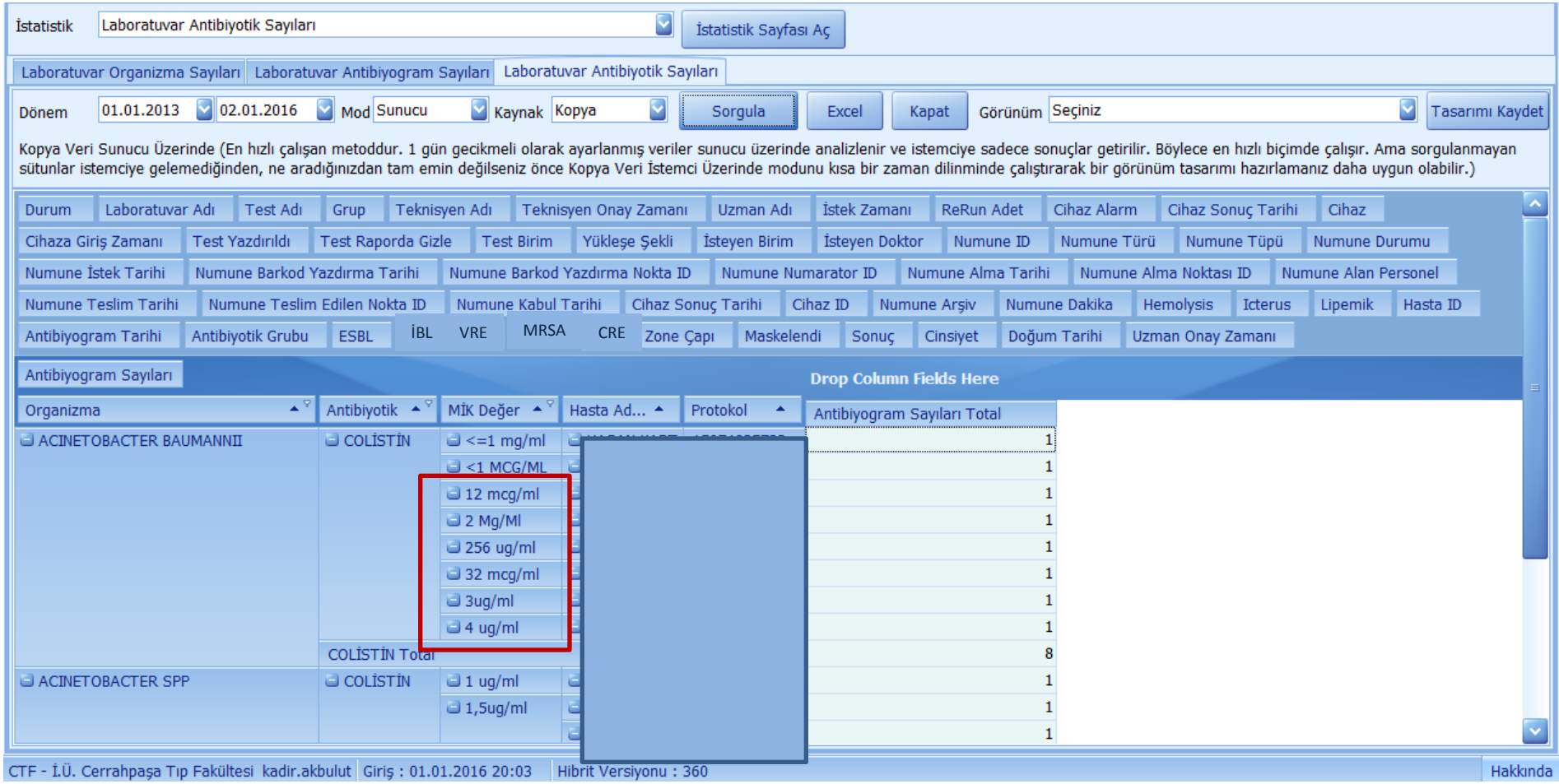
Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria nearest whole mm			MIC Interpretive Criteria (µg/mL)		
			S	I	R	S	I	R
PENICILLINS								
B	Piperacillin	100 µg	≥21	18–20	≤17	≤16	32–64	≥128
O	Mezlocillin	75 µg	≥21	18–20	≤17	≤16	32–64	≥128
O	Ticarcillin	75 µg	≥20	15–19	≤14	≤16	32–64	≥128
β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS								
A	Ampicillin-sulbactam	10/10 µg	≥15	12–14	≤11	≤8/4	16/8	≥32/16
B	Piperacillin-tazobactam	100/10 µg	≥21	18–20	≤17	≤16/4	32/4–64/4	≥128/4
B	Ticarcillin-clavulanic acid	75/10 µg	≥20	15–19	≤14	≤16/2	32/2–64/2	≥128/2
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)								
A	Ceftazidime	30 µg	≥18	15–17	≤14	≤8	16	≥32
B	Cefepime	30 µg	≥18	15–17	≤14	≤8	16	≥32
B	Cefotaxime	30 µg	≥23	15–22	≤14	≤8	16–32	≥64
B	Ceftriaxone	30 µg	≥21	14–20	≤13	≤8	16–32	≥64
CARBAPENEMS								
A	Imipenem	10 µg	≥16	14–15	≤13	≤4	8	≥16
A	Meropenem	10 µg	≥16	14–15	≤13	≤4	8	≥16
LIPOPEPTIDES								
O	Polymyxin B	–	–	–	–	≤2	–	≥4
O	Colistin		–	–	–	≤2	–	≥4

Table 2B-2. Zone Diameter and MIC Interpretive Standards for *Acinetobacter* sp

MİK≤ 2 µg/mL→ DUYARLI

MİK ≥ 4 µg/mL → DİRENÇLİ

CTF: Son iki yılda kolistin MİK > 2 μg/mL 5 A. baumannii olgusu



Enfeksiyon Hastalıkları AD Lab'da Kol R Acinetobacter Ø

OLGU 1.

55 E

BPH

TUR-P planlanıyor

Preoperatif idrar kültürü

ESBL E.coli

Protokol No	:3	**Laboratuvar No**	:4968
TC Kimlik No	:3	**Gönderildiği Tarih**	:13.02.2015
Ad Soyad	:S	**Numune Barkodu**	:3523203
Doğum Tarihi	:03.03.1959	**Gönderen Birim**	:KLİNİK - ÜROLOJİ 2. SERVİS
Yaş / Cinsiyet	:55 / E	**Gönderilen Madde**	:İdrar (HBYS)
Numune Zamanı	:13.02.2015 16:59	**Kabul Zamanı**	:13.02.2015 17:05

İŞLEM	**AÇIKLAMA**
Gram Boyama İle	Bol lökosit görüldü Gram negatif çomaklar görüldü.
İdrar Kültürü	
Koloni Sayımı	100.000
Üreyen Organizmalar	**Escherichia coli** **Genişletilmiş spektrumlu beta-laktamaz yapan bakteri.** *Bakteri Tanımlaması ve Duyarlılık Testi (Antibiyogram) : **[1]***

BAKTERİ TANIMLAMASI VE DUYARLILIK TESTİ

	[1]		[1]		[1]
AMIKACIN	S	SEFTRİAKSON	R	DOKSISIKLIN	-
AMOKCILLIN/KLAVULONAT	S	SEFUROKSIM	R	FOSFOMİSİN	-
AMPICILLIN - SULBACTAM	S	CEFEPIME	R	CEFOXITIN	-
SEFTAZIDIM	S	TRIMETOPRIMSULFAMETOKSAZOL	R	LEVOFLOKSASİN	-
SIPROFLOKSASIN	S	AMPICILLIN	-	MOXIFLOKSASIN	-
GENTAMISIN	S	AZITHROMYCIN	-	NALIDIXIC ASIT	-
ERTAPENEM	S	SEFDİNİR	-	NETİLMİSİN	-
İMİPENEM	S	SEFOPERAZON	-	SEFAPERAZON - SULBACTAM	-
MEROPENEM	S	COLİSTİN	-	TETRASİKLİN	-
NITROFURANTION	S	SEFOTAKSIM	-	TİGESİGLİN	-
PİPERASİLİN/TAZOBAKTAM	S	DORIPENEM	-	TOBRAMISIN	-
AZTREONAM	R				

(R : Dirençli I : Orta Derece Duyarlı S : Duyarlı)

OLGU 1.

T.C.
İstanbul Üniversitesi
Cerrahpaşa Tıp Fakültesi
KONSÜLTASYON

Protokol		**Kimlik No**	39604212748	**Doğum Tarihi**	03.03.1959
Ad Soyad				**Yaş / Cinsiyet**	56 / E

İstek Tarih	13.02.2015	**İsteyen Birim**	ÜROLOJİ 2. SERVİS	**İsteyen Doktor**	
Konsültasyon Tarih	13.02.2015	**Birim**	ENFEKSİYON HASTALIKLARI KONSÜLTASYON HEKİMLİĞİ	**Doktor**	

HASTA BİLGİ : BPH NEDENİYLE TUR-P PLANLANAN HASTANIN GÖNDERİLEN İKAB INDA BOL LÖKOSİT GRAM(-) ÇOMAK GÖRÜLMÜŞTÜR. TARAFINIZCA DEĞERLENDİRİLMESİ RİCA OLUNUR.

AÇIKLAMA : GD İYİ,VİTALLER NORMAL.
1 AYDIR FOLEY SONDA +, ÜRİNER SEMPTOM - ANTIBIYOTIK KULLANIM IOLMAYAN- AKUT FAZ NORMAL OLAN VE SONDA DEGISIMI SONRASI IK ALINAN HASTAYA MONUROL SAŞE 1*1 VERILMESI, 2 GÜN SONRA KONTROL IK VE REKONS ÖNERİLRİ.

OLGU 1.

T.C. İstanbul Üniversitesi
Cerrahpaşa Tıp Fakültesi
Sağlık Uygulama ve Araştırma Merkezi
Tıbbi Mikrobiyoloji Laboratuvarı

Bakteriyoloji Raporu

Protokol No	:	**Laboratuvar No**	: 5052
TC Kimlik No	:	**Gönderildiği Tarih**	: 15.02.2015
Ad Soyad	:	**Numune Barkodu**	: 3524832
Doğum Tarihi	:	**Gönderen Birim**	: KLİNİK - ÜROLOJİ 2. SERVİS
Yaş / Cinsiyet	: 55 / E	**Gönderilen Madde**	: İdrar (HBYS)
Numune Zamanı	: 15.02.2015 07:29	**Kabul Zamanı**	: 15.02.2015 07:32

İŞLEM	AÇIKLAMA
Gram Boyama İle	Az sayıda "epitel hücreleri" Az sayıda lökositler Mikroorganizma görülmedi
İdrar Kültürü	
Üreyen Organizmalar	Bakteri üremedi

OLGU 1.

T.C.
İstanbul Üniversitesi
Cerrahpaşa Tıp Fakültesi
AMELİYAT RAPORU

Protokol		**Kimlik No**	39604212748	**Doğum Tarihi**	03.03.1959
Ad Soyad				**Yaş / Cinsiyet**	56 / E

TARİH : 16.02.2015 14:26, **DEFTER NO :** 20152094

AMELİYAT EKİBİ :
OPERATÖR : Prof.Dr. ZÜBEYR TALAT,
OPERATÖR : Dr. ABULFAZ ABBASLI,
OPERATÖR : Dr. FAHRİ YAVUZ İLKİ,
ANESTEZİST : Uzman Hekim BİRSEL EKİCİ

AMELİYAT		KESİ	SAĞ / SOL
621390	PROSTATEKTOMI, UNIPOLAR TUR (621390)	1	3
619530	SISTOSKOPI,TANISAL (619530)	1	3

AMELİYAT ÖNCESİ : BPH

ANESTEZİ : SPİNAL

AMELİYAT NOTU : HASTA SAA LİTOTOMİ POZİSYONUNDA YATIRILDI. USULÜNE UYGUN SİLME VE ÖRTME İŞLEMLERİNDEN SONRA SİSTOSKOP İLE MESANEYE GİRİLDİ. BİLATERAL ÜRETER ORİFİSLERİ GÖRÜLDÜ. MESANE KARŞI DUVARDA KUBBEYE DOĞRU YÜZEYEL PAPİLLER TÜMÖRAL OLUŞUMLAR GÖRÜLDÜ.REZEKSİYON BİYOPSİSİ ALINDI.PROSTAT LATERAL LOBLARININ ÜRETRAYI KAPATTIĞI VE MEDİAN LOB MEVCUDİYETİ SAPTANDI. HASTAYA VERUMONTANUM KORUNARAK TUR-P UYGULANDI. PARÇALARIN TEMİZLENMESİ VE KANAMA KONTROLÜ ARDINDAN 3 YOLLU 22 FR SONDA TAKILARAK İŞLEME SON VERİLDİ.8 ADET REZECTİSOL 3000 KULLANILDI.621390

AMELİYAT SONU : TUR-P

OLGU 1.

T.C. İstanbul Üniversitesi
Cerrahpaşa Tıp Fakültesi
Sağlık Uygulama ve Araştırma Merkezi
Tıbbi Mikrobiyoloji Laboratuvarı

Bakteriyoloji Raporu

Protokol No	:	**Laboratuvar No**	: 7569
TC Kimlik No	:	**Gönderildiği Tarih**	: 09.03.2015
Ad Soyad	:	**Numune Barkodu**	: 3622404
Doğum Tarihi	: 03.03.1959	**Gönderen Birim**	: POLİKLİNİK - ÜROLOJİ POLİKLİNİK
Yaş / Cinsiyet	: 56 / E	**Gönderilen Madde**	: İdrar (HBYS)
Numune Zamanı	: 09.03.2015 10:47	**Kabul Zamanı**	: 09.03.2015 11:01

İŞLEM	**AÇIKLAMA**
Gram Boyama İle	Gram negatif çomaklar
İdrar Kültürü	
Koloni Sayımı	10000
Üreyen Organizmalar	**Acinetobacter baumannii üredi.** *Bakteri Tanımlaması ve Duyarlılık Testi (Antibiyogram) :* ***[1]***

BAKTERİ TANIMLAMASI VE DUYARLILIK TESTİ

	[1]		[1]
AMIKACIN	R	SEFOTAKSIM	-
SEFTAZIDIM	R	DORIPENEM	-
SIPROFLOKSASIN	R	DOKSISIKLIN	-
GENTAMISIN	R	TİKARSİLİN	-
COLİSTİN	R MİK:3ug/ml	LEVOFLOKSASİN	-
SEFTRİAKSON	R	MOXIFLOKSASIN	-
CEFEPIME	R	NETİLMİSİN	-
İMİPENEM	R	NORFLOKSASIN	-
MEROPENEM	R	NITROFURANTION	-
PİPERASİLİN/TAZOBAKTAM	R	RIFAMPISIN	-
AZTREONAM	-	SEFAPERAZON - SULBACTAM	-
PIPERACILLIN	-	TETRASİKLİN	-
AMPICILLIN - SULBACTAM	-	TİGESİGLİN	-
KLORAMFENIKOL	-	TOBRAMISIN	-
SEFOPERAZON	-	TRIMETOPRIMSULFAMETOKSAZOL	-

(**R** : Dirençli **I** : Orta Derece Duyarlı **S** : Duyarlı)

Postop 24. gün
idrar kültürü
Kolistin Dirençli A. Baumannii
MİK 3 mcg/mL
10 bin kob/mL

TEDAVİ VERİLMEDİ

OLGU 2.

57 K
Over ca
Terminal dönem
Ascites
Parasentez
kültürü

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Bakteriyoloji Raporu

Protokol No	:	**Laboratuvar No**	:
TC Kimlik No	:	**Gönderildiği Tarih**	: 26.07.2015
Ad Soyad	:	**Numune Barkodu**	: 4222974
Doğum Tarihi	: 20.09.1957	**Gönderen Birim**	: KADIN DOĞ.JİNEKO-ONKO.2.KAT
Yaş / Cinsiyet	: 57 / K	**Gönderilen Madde**	: Yara
Numune Zamanı	: 26.07.2015 01:09	**Kabul Zamanı**	: 26.07.2015 01:09

İŞLEM	**AÇIKLAMA**
Gram Boyama İle	Lökositler görüldü
	Gram negatif çomaklar
Yara Kültürü	
Üreyen Organizmalar	**Acinetobacter baumannii üredi.** *Bakteri Tanımlaması ve Duyarlılık Testi (Antibiyogram) :* ***[1]***
	Escherichia coli *Bakteri Tanımlaması ve Duyarlılık Testi (Antibiyogram) :* ***[2]***
Not	Acinetobacter için tigesiklin MIK değeri 12 ug/ml

BAKTERİ TANIMLAMASI VE DUYARLILIK TESTİ

	[1]	[2]
AMIKACIN	R	S
SEFTAZIDIM	R	S
SIPROFLOKSASIN	R	S
GENTAMISIN	R	S
İMİPENEM	R	S
MEROPENEM	R	S
PİPERASİLİN/TAZOBAKTAM	R	S
AZTREONAM	-	S
SEFOTAKSIM	-	S
SEFUROKSIM	-	S
ERTAPENEM	-	S
CEFEPIME	-	S
AMOKCILLIN/KLAVULONAT	-	R
AMPICILLIN	-	R

	[1]	[2]
COLİSTİN	R MİK:4 ug/ml	-
NETİLMİSİN	R	-
PIPERACILLIN	-	-
AMPICILLIN - SULBACTAM	-	-
AZITHROMYCIN	-	-
KLORAMFENIKOL	-	-
SEFDİNİR	-	-
CEFIXIME	-	-
SEFOPERAZON	-	-
SEFTRİAKSON	-	-
DORIPENEM	-	-
DOKSISIKLIN	-	-
FOSFOMİSİN	-	-

	[1]	[2]
CEFOXITIN	-	-
TİKARSİLİN	-	-
LEVOFLOKSASİN	-	-
MOXIFLOKSASIN	-	-
NALIDIXIC ASIT	-	-
NORFLOKSASIN	-	-
NITROFURANTION	-	-
RIFAMPISIN	-	-
SEFAPERAZON - SULBACTAM	-	-
TETRASİKLİN	-	-
TİGESİGLİN	-	-
TOBRAMISIN	-	-
TRIMETOPRIMSULFAMETOKSAZOL	-	-

(**R** : Dirençli **I** : Orta Derece Duyarlı **S** : Duyarlı)

Prof.Dr. Murat GÜNAYDIN

OLGU 2. E.Coli için Pip/tazo + AK, Acinetobacter için tedavi Ø

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KONSÜLTASYON

Protokol		**Kimlik No**	21350152256	**Doğum Tarihi**	20.09.1957
Ad Soyad				**Yaş / Cinsiyet**	58 / K

İstek Tarih	28.07.2015	**İsteyen Birim**	KADIN DOĞ.JİNEKO-ONKO.2.KAT	**İsteyen Doktor**	
Konsültasyon Tarih	28.07.2015	**Birim**	ENFEKSİYON HASTALIKLARI KONSÜLTASYON HEKİMLİĞİ	**Doktor**	

HASTA BİLGİ : 58 YAŞINDA OVER CA DESTEK HASTASI ÖNCESİNDE 6 GÜN PİPERASİLİN+TAZOBAKTAM KULLANAN VE TEDAVİ ALTINDA GENEL DURUMU BOZULAN CRP'Sİ ARTAN HASTANIN ANTİBİYOTERAPİSİ TEKRAR DÜZENLENMİŞ VE YOĞUN BAKIMA GÖNDERİLMİŞTİR. 11. GÜNÜNDE İMİPENEM 4*500 VE AMİKASİN 2*500 KULLANAN PARASENTEZ KÜLTÜRÜNDE İMİPENEM DİRENÇLİ KARBAPENEMAZ ÜRETEN E. COLİ ÜREMİŞ OLUP TARAFINIZCA DEĞERLENDİRİLMESİ RİCA OLUNUR.

AÇIKLAMA : KARBAPENAMAZ YAPAN E.COLİ ÜREMESİ OLAN HASTAYA CİDDİ TEMAS İZOLYASYONU UYGULANMASI GEREKMEKTEDİR!!!
ÖNERİLER:
-HASTANIN İMİPENEM TEDAVİSİNİN KESİLMESİ.
-TEDAVİSİNİN PİPERACİLLİN TAZOBAKTAM 4X4.5GR VE AMİKACİN 1X1GR OLARAK DÜZENLENMESİ.
-ATEŞ OLMASA DA 2 HK GÖNDERİLMESİ.
-MİKROBİYOLOJİYLE KONUŞILARAK COLİSTİN DUYARLILIĞININ ÇALIŞILMASININ İSTENMESİ.
-GÜNLÜK AKUT FAZ TAKİBİ YAPILMASI.
-YARINA PROKALSİTONİN İSTENMESİ.

Kolistin MİK istendi

	[1]	[2]
AMIKACIN	R	S
SEFTAZIDIM	R	S
SIPROFLOKSASIN	R	S
GENTAMISIN	R	S

	[1]
COLİSTİN	R MİK:4 ug/ml
NETİLMİSİN	R
PIPERACILLIN	-
AMPICILLIN - SULBACTAM	-

OLGU 2.

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Fikret Biyal Merkez Araştırma Laboratuvarı

Protokol No		**TC Kimlik No**	21350152256
Hasta Ad Soyad		**Laboratuar No**	**1661941**
Doğum Tarihi	20.09.1957	**Cinsiyet / Yaş**	K / 58
Gönderen Birim	YOĞUN BAKIM - KADIN DOĞ.JİNEKO-ONKO.2.KAT	**Gönderildiği Tarih**	29.07.2015

Örnek : **4238732**; Serum; 29.07.2015 11:02; Kabul : **29.07.2015 11:56**; Sonuç : **29.07.2015 14:58**

Tetkik	Sonuç		Birim	Referans Değer	Açıklama
Prokalsitonin	**1,776**	**H**	ng/ml	0 - 0,5	

29.07.2015 14:58:09

Protokol No	: 21350152256	**Laboratuvar No**	: 16235
TC Kimlik No	: 21350152256	**Gönderildiği Tarih**	: 28.07.2015
Ad Soyad	: HATİCE DERAL	**Numune Barkodu**	: 4235523
Doğum Tarihi	: 20.09.1957	**Gönderen Birim**	: YOĞUN BAKIM - KADIN DOĞ.JİNEKO-ONKO.2.KAT
Yaş / Cinsiyet	: 57 / K	**Gönderilen Madde**	: Hemokültür
Numune Zamanı	: 28.07.2015 17:29	**Kabul Zamanı**	: 28.07.2015 17:40

İŞLEM	AÇIKLAMA
Kan Kültürü,Aerop (Otomatize sistem)	
Üreyen Organizmalar	5 günlük inkübasyonla bakteri üremedi.

Kolistin (R) + Tigesiklin (S? R?) → kontrol kültür → üreme olmadı

OLGU 2.

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KONSÜLTASYON

Protokol		**Kimlik No**	21350152256	**Doğum Tarihi**	20.09.1957
Ad Soyad				**Yaş / Cinsiyet**	58 / K

İstek Tarih	13.08.2015	**İsteyen Birim**	KADIN DOĞ.JİNEKO-ONKO.2.KAT	**İsteyen Doktor**	
Konsültasyon Tarih	13.08.2015	**Birim**	ANESTEZİYOLOJİ KONS.HEKİMLİĞİ	**Doktor**	

HASTA BİLGİ : 58 Y, OVER CA DESTEK HASTASI TERMİNAL DÖNEM GENEL DURUMKÖTÜ OLAN ARTER KAN GAZI ALINAN HASTANIN YOĞUN BAKIM ENDİKASYONU AÇISINDAN TARFINIZCA DEĞERLENDİRİLMESİ RİCA OLUNUR.

AÇIKLAMA : HASTA SAAT 23.15 DE KADIN DOGUM SERVISINDE ODASINDA GORULDU. 58 YASINDA BAYAN BHASTA BILINEN NUKS OVER CANSERI VE MULTIPLE METASTAZLARI MEVCUT. HASTANIN MEVCUT SOLUNUM YETMEZLIGI NEDNENIYLE TARAFIMIZCA 26.07.15 TARIHINDEDE DEGERLENDIRILMIS OLUP YBU ENDIKASYONU KONMUSUDR. HASTA VE YAKINLARI YBU YATIRILMASINI KABUL EDMEMESI SONUCU SERVISTE TAKIPLERI DEVAM ETMISDIR. BUGUN SOLUNUM YETMEZLIGI ARTMIS OLUP VE HASTA YAKINLARININ YBU TRANSFERI KABUL ETMESI UZERINE TARAMIZCA TEKRARDAN KONSULTE EDILDI. FM DE SUURU ACIK KOOPERE SOLUNUM SESLERI BILATERAL SEKRETUAR BATIN TAHTA KARIN. TA 140/70 KAH 130/DK SPO2 78 DSS 30/DK AKG PCO2 56 PO2 59 PH 7.37 LAC 1.2 BE 6.4 HCO3 32 SO2 91. HASTA OTE EDILDI. CTF YBU DE YER OLMAMASI NEDENIYLE DIS YBU TRANSFERI UYGUNDUR. ŞIŞLI KOLON HAST YBU NE KABUL EDILMIS OLUP AMBULANS BEKLENMEKTEDIR.
HASTA SAAT 23.30 KARDIAK AREST OLDU. CPR BASLANDI. 40DK CPR SONUCUNDA SAAT 00.10 DA SPONTAN DOLASIM SAGLANAMAMASI SONUCU EXITUS OLARAK KABUL EDILDI.

OLGU 3.

56 K
Ekim 2015→
Mesh ile abdominal herni onarımı
4 yıldır
Ara ara enfeksiyon
Cerrahi revizyonlar
2015→ Kol R AB

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Bakteriyoloji Raporu

Protokol No	:	**Laboratuvar No**	:
TC Kimlik No	:	**Gönderildiği Tarih**	: 26.11.2015
Ad Soyad	:	**Numune Barkodu**	: 4743984
Doğum Tarihi	: 21.05.1959	**Gönderen Birim**	: ACİL POLİKLİNİK
Yaş / Cinsiyet	: 56 / K	**Gönderilen Madde**	: Yara
Numune Zamanı	: 26.11.2015 20:29	**Kabul Zamanı**	: 26.11.2015 21:35

İŞLEM	AÇIKLAMA
Gram Boyama İle	Gram negatif çomaklar Gram pozitif koklar Epitel hüceleri görüldü
Yara Kültürü	
Üreyen Organizmalar	**Escherichia coli** **Genişletilmiş spektrumlu beta-laktamaz yapan bakteri.** *Bakteri Tanımlaması ve Duyarlılık Testi (Antibiyogram) :* ***[1]***
	Acinetobacter baumannii üredi. *Bakteri Tanımlaması ve Duyarlılık Testi (Antibiyogram) :* ***[2]***
Not	Colistin E testi ayrı bildirilecektir.
Anaerob Kültür	
Anerop Üreyenler	Bakteri üremedi

BAKTERİ TANIMLAMASI VE DUYARLILIK TESTİ

	[1]	[2]		[1]	[2]
AMIKACIN	S	R	AZTREONAM	R	-
GENTAMISIN	S	R	AMOKCILLIN/KLAVULONAT	R	-
MEROPENEM	S	R	AMPICILLIN	R	-
PİPERASİLİN/TAZOBAKTAM	S	R	COLİSTİN	-	R (MİK:12 mcg/m
ERTAPENEM	S	-	SEFTRİAKSON	R	-
İMİPENEM	S	-	SEFUROKSIM	R	-
TİGESİGLİN	S	-	NETİLMİSİN	-	R
PIPERACILLIN	R	R	SEFOTAKSIM	-	-
SEFTAZIDIM	R	R	LEVOFLOKSASİN	-	-
SIPROFLOKSASIN	R	R	NORFLOKSASIN	-	-
CEFEPIME	R	R	NITROFURANTION	-	-
TRIMETOPRIMSULFAMETOKSAZOL	R	R	TOBRAMISIN	-	-

(R : Dirençli I : Orta Derece Duyarlı S : Duyarlı)

OLGU 3.

4 yıl önce...

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EPİKRİZ

Protokol		**Doğum Tarihi**	21.05.1959
Ad Soyad		**Yaş / Cinsiyet**	56 / K

Tarih	29.11.2011	**Birim**	ACİL GÖZLEM SERVİSİ	**Doktor**	
Ameliyat Tarihi		**Takip Eden Doktor**		**Yatıran Doktor**	
Eşlik Eden Hastalık	VAR				
Komplikasyon	VAR				
Yatırılış Nedeni	TETKİK	**Yatış Çıkış Tarihleri**	29.11.2011	**Dosya No**	
TANI	R10 - Abdominal ve pelvik ağrı (Birincil Tanı) (Kesin Tanı)				
ŞİKAYET : KARIN AĞRISI					
HİKAYE : KARIN AĞRISI ŞİKAYETİ İLE HASTA TARAFIMIZA BAŞVURDU.					
ÖZGEÇMİŞ : ÖZELLİK YOK					
SOYGEÇMİŞ : ÖZELLİK YOK					
GEÇİRDİĞİ AMELİYATLAR : YOK					
SÜREKLİ KULLANDIĞI İLAÇLAR : YOK					
ALIŞKANLIKLARI : YOK					
KLİNİK GİDİŞ VE SONUÇ : HASTA DEĞERLENDİRİLDİ.BATIN TÜM KADRANLARDA HASSASİYET MEVCUT.HASTAYA BATIN BT ÇEKİLDİ: İNSİZYON HATTI BOYUNCA CİLTALTI 13*4*13 CMLİK KOLEKSİYON SAPTANDI. AMOKLAVİN BAŞLANAN HASTA BT SONUCU İLE POLİKLİNİK KONTROLÜNE GELMEK ÜZERE TABURCU EDİLDİ.					

Postop 1. ayda insizyon hattında koleksiyon→ kültür alınmadan→ Ko-amoksiklav

OLGU 3.

26.10.2015→ İnsizyonel herni→Mesh ile onarım→sefazol alerjisi → AB değişikliği?

TARİH : 26.10.2015 15:45, **DEFTER NO :** 20156265			
AMELİYAT EKİBİ : OPERATÖR : OPERATÖR : ANESTEZİST			
AMELİYAT		KESİ	SAĞ / SOL
603801	GREFTLI INSIZYONEL HERNI ONARıMı (603801)		
AMELİYAT ÖNCESİ : İNSİZYONEL HERNİ			
ANESTEZİ : GENEL			
AMELİYAT NOTU : GAA HASTA SUPİN POZİSYONDA MASAYA ALINDI. USULÜNE UYGUN ŞEKİLDE BOYANIP ÖRTÜLDÜ. GA MEDİAN VE VERTİCAL BALIK AĞZI İNSİZYONLA CİLT VE CİLT ALTI GEÇİLDİ.SAĞLAM FASYA ÜSTÜ SERBESTLENDİ. FITIK KESESİ EKSİZE EDİLDİ. 1.0 PDS İLE DEFEKT KAPATILDI. ÜSTÜNE UYGUN BOYUTLARDA KESİLEN PROLEN MESH ONLEY OLARAK 1.0 PROLEN İPLERLE SABİTLENDİ. YAPILAN KANAMA KONTROLÜNÜN ARDINDAN İNSİZYON ALTINA İKİ ADET HEMOVACK DREN YERLEŞTİRİLDİ. CİLT VE CİLT ALTI USULÜNE UYGUN ŞEKİLDE KAPATILDI. YAPILAN PANSUMANIN ARDINDAN OPERASYONA SON VERİLDİ.			
AMELİYAT AÇIKLAMA : PROLEN MESH İLE ONLEY TARZI İNSİZYONEL HERNİ TAMİRİ			
AMELİYAT SONU : PROLEN MESH İLE ONLEY TARZI İNSİZYONEL HERNİ TAMİRİ			

OLGU 3.

Protokol		**Doğum Tarihi**	21.05.1959
Ad Soyad		**Yaş / Cinsiyet**	56 / K

İstek Tarih	31.10.2015	**İsteyen Birim**	GENEL CER.GORBON SER.A BLOK	**İsteyen Doktor**	
Konsültasyon Tarih	31.10.2015	**Birim**	ENFEKSİYON HASTALIKLARI KONSÜLTASYON HEKİMLİĞİ	**Doktor**	

HASTA BİLGİ : 52 K ABDOMİNOPLASTİ+ ONLAY PROLEN MESH İLE İNSİZYONEL HERNİ TAMİRİ YAPILAN HASTANIN SEFAZOL TEDAVİSİ ALTINDA AKUT FAZLARINDA ARTIŞ MEVCUT. SEFAZOL ALERJİSİ GELİŞEN HASTANIN ANTİBİYOTERAPİSİ AÇISINDAN DEĞERLENDİRİLMESİ RİCA OLUNUR.

AÇIKLAMA : hasta yatağında değ gd iyi şuur açık koopere oryente
ateş:38 nds:88 dss:22 ta:100/60
batında insizyon hattında yer yer pürülan akıntı mevcut
defans ribaund yok
düz sefazol sonrası dil ve yüzde şişme olmuş
öneriler:
+hastadan 2hk alınması, tit gönderilmesi
+abse-kolleksiyon-fistül açısından batın görüntüleme yapılması(gereğinde drenaj ve kültür örneklemnin sağlanması)
+tigesiklin 1x100 mg iv yükleme 12 saat sonra 2x50 mg iv idame başlanması
+hemogram crp üre kre takibi
+kültür sonuç takibi önerilir saygıalrımla

OLGU 3.

TIG kesilmiş, Cipro+metronidazol altında →1 ay sonra tekrar baş vuru → 4x2 cm koleksiyon

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KONSÜLTASYON

Protokol		**Doğum Tarihi**	21.05.1959
Ad Soyad		**Yaş / Cinsiyet**	56 / K

İstek Tarih	26.11.2015	**İsteyen Birim**	ACİL GÖZLEM SERVİSİ	**İsteyen Doktor**	
Konsültasyon Tarih	26.11.2015	**Birim**	ENFEKSİYON HASTALIKLARI KONSÜLTASYON HEKİMLİĞİ	**Doktor**	

HASTA BİLGİ : 56 YAŞ KADIN HASTA, İNSİZYONEL HERNİ NEDENİYLE 26.10.2015 TARİHİNDE MESH İLE TAMİR YAPILAN POSTOP DÖNEMDEN İTİBAREN BAŞLAYAN YARADA AYRIŞMA VE AKINTISI OLAN HASTANIN SON 2 GÜNDÜR BAŞLAYAN YARA YERİNDE AĞRI OLMASI NEDENİYLE TARAFIMIZA BAŞVURDU. ORAL OLARAK CİPRO, FLAGYL KULLANDIĞINI BELİRTEN, ATEŞİ:37.5 GÖNDERİLEN RUTİN TETKİKLERDE WBC:14,1 , NEU%48,3, CRP:37,8 GELEN YAPTIRILAN YÜZEYEL USGDE YARA CEVRESİNDE YAYGIN SELÜLİT GÖRÜNÜMÜ VE CİLTTEN 2 CM DERİNDE 4*2CMLİK YOĞUN İÇERİKLİ KOLEKSİYON SAPTANMIŞTIR. TARAFINIZDAN DEĞERLENDİRİLMESİ RİCA OLUNUR.

AÇIKLAMA : KOLEKSİYON ALANINDAN DRENE EDİLEREK AEROB VE ANAEROB KÜLTÜR ALINDIKTAN SONRA PİPERACİLLİN MEVCUT TEDAVİLERİN KESİLMESİ.
TYGECİKLİN 1X100MG YÜKLEME 2X50MG İDAME BAŞLANMASI
ODAK KONTROLÜ AÇISINDAN YAPILABİLECEKLERİN YAPILMASI
KÜLTÜR SONUCUYLA REKONSU ÖNERİLİR.
NOT: TYGECİKLİN E-REÇETE KODU : J2PJFZ (DIŞ ECZANEDEN ALINACAK)

OLGU 3.

Protokol		**Doğum Tarihi**	21.05.1959
Ad Soyad		**Yaş / Cinsiyet**	56 / K

İstek Tarih	06.01.2016	**İsteyen Birim**	ACİL POLİKLİNİK	**İsteyen Doktor**	
Konsültasyon Tarih	07.01.2016	**Birim**	ENFEKSİYON HASTALIKLARI KONSÜLTASYON HEKİMLİĞİ	**Doktor**	

HASTA BİLGİ : 56 YAŞ KADIN HASTA, İNSİZYONEL HERNİ NEDENİYLE 26.10.2015 TARİHİNDE MESH İLE TAMİR YAPILAN POSTOP DÖNEMDEN İTİBAREN BAŞLAYAN YARADA AYRIŞMA VE AKINTISI OLAN HASTANIN SON 2 GÜNDÜR BAŞLAYAN YARA YERİNDE AĞRI OLMASI NEDENİYLE TARAFIMIZA BAŞVURDU. ORAL OLARAK CİPRO, FLAGYL KULLANDIĞINI BELİRTEN, ATEŞİ:37.5 GÖNDERİLEN RUTİN TETKİKLERDE WBC:18.1 CRP:51 BULUNMUŞTUR.YAPILAN US:İNSİZYON HATTI SUPEROLATERALİNDE CİLT ALTINDA 52X34 MM LİK LOKULE KOLLEKSİYON İZLENMİŞTİR.HASTANIN TARFINIZCA DEĞERLENDİRİLMESİ RİCA OLUNUR.

AÇIKLAMA : 56 Y/K HASTA, İNSİZYONEL HERNİ NEDENİYLE 26.10.2015 TARİHİNDE MESH İLE TAMİR YAPILMIŞ. POSTOP DÖNEMDEN İTİBAREN BAŞLAYAN YARADA AYRIŞMA VE AKINTISI VAR.
SON 2 GÜNDÜR BAŞLAYAN YARA YERİNDE AĞRI OLMASI NEDENİYLE BAŞVURMUŞ. ORAL OLARAK CİPRO, FLAGYL KULLANIYOR.ATEŞİ:37.5 GÖNDERİLEN RUTİN TETKİKLERDE WBC:18.1 CRP:51
YAPILAN USG:İNSİZYON HATTI SUPEROLATERALİNDE CİLT ALTINDA 52X34 MM LİK LOKULE KOLLEKSİYON İZLENMİŞ.BU SEBEPLE DANIŞILDI
ÖNERİLER:
1.2HK+İK+APSE BOŞALTILARAK AEROB/ANAEROB KX GÖNDERİLMESİ,
2.SULPERAZON 2*2 GİV + TYGACİL 1*100 MG YÜKLEME 2*50MG İV İDAME BAŞLANMASI,
3.YAKIN GD/ANT/CRP/PROKALSITONIN/HEMOGRAM/KX SONUÇLARININ TAKIBI,
4.GEREĞİNDE REKONS.

Cerrahi tarafından ayaktan takip ediliyor. TIG+sulperazon ile bulgular geriledi. Acinetobacter tekrar üremedi. Riskler konuşuldu birlikte takibi planlandı.

OLGU 4.

ACİL CERRAHİ 40 E Şarapnel yaralanması, humerus + tibia kırığı, eksternal fiksatör, ileal rezeksiyon

Yaş / Cinsiyet : 40 / E
Gönderilen Madde : Balgam
Numune Zamanı : 30.07.2015 07:14
Kabul Zamanı : 30.07.2015 07:35

İŞLEM	AÇIKLAMA
Balgam Kültürü	
Üreyen Organizmalar	**Metisiline dirençli S. aureus**
	*Bakteri Tanımlaması ve Duyarlılık Testi (Antibiyogram) : **[1]***
	Acinetobacter baumannii üredi.
	*Bakteri Tanımlaması ve Duyarlılık Testi (Antibiyogram) : **[2]***

Balgam kaliteli değil, Oral kolonizasyon, Temas izolasyonu

BAKTERİ TANIMLAMASI VE DUYARLILIK TESTİ

	[1]	[2]		[1]	[2]		[1]	[2]
TRIMETOPRIMSULFAMETOKSAZOL	S	R	NETİLMİSİN	-	R	CEFOXITIN	-	-
KLINDAMISIN	S	-	PİPERASİLİN/TAZOBAKTAM	-	R	TİKARSİLİN	-	-
ERYTROMYCIN	S	-	AZTREONAM	-	-	İMİPENEM	-	-
LİNEZOLİD	S	-	AMPICILLIN	-	-	LEVOFLOKSASİN	-	-
TEIKOPLANIN	S	-	AMPICILLIN - SULBACTAM	-	-	METISILIN	-	-
VANKOMYCIN	S	-	KLORAMFENIKOL	-	-	MOXIFLOKSASIN	-	-
DAPTOMYCIN	S	-	SEFOPERAZON	-	-	NORFLOKSASIN	-	-
PIPERACILLIN	-	R	COLİSTİN	-	R MİK:32 mcg/ml	NITROFURANTION	-	-
AMIKACIN	-	R	SEFTRİAKSON	-	-	RIFAMPISIN	-	-
SEFTAZIDIM	-	R	SEFOTAKSIM	-	-	SEFAPERAZON - SULBACTAM	-	-
SIPROFLOKSASIN	-	R	DORIPENEM	-	-	CEFAZOLIN	-	-
GENTAMISIN	-	R	DOKSISIKLIN	-	-	TETRASİKLİN	-	-
CEFEPIME	-	R	FUSİDİK ASİT	-	-	TİGESİGLİN	-	-
MEROPENEM	-	R	FOSFOMİSİN	-	-	TOBRAMISIN	-	-

OLGU 4.

Kontrol kültürlerde Acinetobacter üremedi

Protokol		**Kimlik No**	39673918220	**Doğum Tarihi**	17.09.1974
Ad Soyad				**Yaş / Cinsiyet**	41 / E

İstek Tarih	07.08.2015	**İsteyen Birim**	ACİL CERRAHİ SERVİSİ	**İsteyen Doktor**
Konsültasyon Tarih	10.08.2015	**Birim**	ENFEKSİYON HASTALIKLARI KONSÜLTASYON HEKİMLİĞİ	**Doktor**

HASTA BİLGİ : 40 YAŞINDA (İMMOBİL) SURUÇTAKİ BOMBALI PATLAMADA HUMERUS VE TİBİA PARÇALI KIRIĞI OLAN(EXTERNAL FİKSASYON UYGULANMIŞ), İLEAL REZEKSİYON YAPILAN, VUCUDUNDA YAYGIN ŞARAPNEL YARALANMALARI OLAN HASTANIN CVK KÜLTÜRÜNDE STAF. HOMİNİS ÜREMESİ OLMULTUR. TARAFINIZCA DEĞERLENDİRİLMESİ RİCA OLUNUR

AÇIKLAMA : TEİKOPLANİN TEDAVİSİ ALTINDA OLAN HASTANIN MEVCUT TEDAVİSİNİN DEVAMI ÖNERİLDİ
EK ÖNERİMİZ BULUNMAMAKTADIR

OLGU 4.

Protokol		**Doğum Tarihi**	17.09.1974
Ad Soyad		**Yaş / Cinsiyet**	41 / E

İstek Tarih	05.10.2015	**İsteyen Birim**	ACİL CERRAHİ SERVİSİ	**İsteyen Doktor**
Konsültasyon Tarih	05.10.2015	**Birim**	ENFEKSİYON HASTALIKLARI KONSÜLTASYON HEKİMLİĞİ	**Doktor**

HASTA BİLGİ : 41 E 2 AY ÖNCE SURUÇTAKİ BOMBALI PATLAMADA HUMERUS VE TİBİA PARÇALI KIRIĞI OLAN(EXTERNAL FİKSASYON UYGULANMIŞ), İLEAL REZEKSİYON YAPILAN(2 AY ÖNCE) VE 21.09.2015 DE OMENTAL NEKROZ NEDENİ İLE OPERASYON YAPILAN HASTA MERONEM 7. GÜNÜDEDİR.WBC:7.8 CRP :4.2 ATEŞİ:36 DERECEDİR.HASTANIN ANTİBİYOTERAPİSİNİN STOPLANMASI AÇISINDAN DEĞERLENDİRİLMESİ RİCA OLUNUR.

AÇIKLAMA : TARAFINIZDAN ODAK KONTROLÜNÜN SAĞLANMASI ŞARTIYLA HASTANIN TEDAVİSİNİN EN AZ 14GÜNE TAMAMLANMASI GEREKMEKTEDİR.

OLGU 5.

38 E

Tip 1 DM

KBY

Renal transplantlı

Diyabetik ayak

Doku kültürü

KOL MİK=256

Bakteriyoloji Raporu

Protokol No	:	**Laboratuvar No**	:16035
TC Kimlik No	:	**Gönderildiği Tarih**	:06.07.2015
Ad Soyad	:	**Numune Barkodu**	:4155135
Doğum Tarihi	:15.05.1977	**Gönderen Birim**	:POLİKLİNİK - PLASTİK CERRAHİ POLİKLİNİĞİ
Yaş / Cinsiyet	:38 / E	**Gönderilen Madde**	:Yara Sürüntüsü
Numune Zamanı	:06.07.2015 19:25	**Kabul Zamanı**	:06.07.2015 19:25

İŞLEM	**AÇIKLAMA**
Gram Boyama İle	Epitel hücreleri görüldü Lökositler görüldü Gram pozitif diplokoklar Gram pozitif çomaklar Gram negatif çomaklar görüldü
	Anaerop etkenli polimikrobiyal enfeksiyon görünümü
Yara Kültürü	
Üreyen Organizmalar	**Escherichia coli** *Bakteri Tanımlaması ve Duyarlılık Testi (Antibiyogram) : [1]*
	Acinetobacter baumannii üredi. *Bakteri Tanımlaması ve Duyarlılık Testi (Antibiyogram) : [2]*
	Metisiline dirençli S. aureus *Bakteri Tanımlaması ve Duyarlılık Testi (Antibiyogram) : [3]*
Anaerob Kültür	
Anerop Üreyenler	Bakteri üremedi

	[1]	[2]	[3]
GENTAMISIN	S	S	S
SIPROFLOKSASIN	S	R	S
AMIKACIN	S	R	-
SEFTAZIDIM	S	R	-
CEFEPIME	S	R	-
İMİPENEM	S	R (MİK:32 ug/ml)	-
MEROPENEM	S	R (MİK:32 ug/ml)	-
TRIMETOPRIMSULFAMETOKSAZOL	R	-	S
PİPERASİLİN/TAZOBAKTAM	S	R	-
AZTREONAM	S	-	-
SEFTRİAKSON	S	-	-
SEFUROKSIM	S	-	-
ERTAPENEM	S	-	-
LİNEZOLİD	-	-	S
SEFAPERAZON - SULBACTAM	-	S	-
TEIKOPLANIN	-	-	S
VANKOMYCIN	-	-	S

	[1]	[2]	[3]
AMPICILLIN	-	-	R
COLİSTİN	-	R (MİK:256 ug/ml)	-
ERYTROMYCIN	-	-	R
PIPERACILLIN	-	-	-
AMOKCILLIN/KLAVULONAT	-	-	-
AMPICILLIN - SULBACTAM	-	-	-
AZITHROMYCIN	-	-	-
KLORAMFENIKOL	-	-	-
SEFDİNİR	-	-	-
CEFIXIME	-	-	-
SEFOPERAZON	-	-	-
SEFOTAKSIM	-	-	-
KLINDAMISIN	-	-	-
DORIPENEM	-	-	-
DOKSISIKLIN	-	-	-
FUSİDİK ASİT	-	-	-

	[1]	[2]	[3]
FOSFOMİSİN	-	-	-
CEFOXITIN	-	-	-
TİKARSİLİN	-	-	-
LEVOFLOKSASİN	-	-	-
METISILIN	-	-	-
MOXIFLOKSASIN	-	-	-
NALIDIXIC ASIT	-	-	-
NETİLMİSİN	-	-	-
NORFLOKSASIN	-	-	-
NITROFURANTION	-	-	-
RIFAMPISIN	-	-	-
CEFAZOLIN	-	-	-
TETRASİKLİN	-	-	-
TİGESİGLİN	-	-	-
TOBRAMISIN	-	-	-
DAPTOMYCIN	-	-	-

(**R** : Dirençli **I** : Orta Derece Duyarlı **S** : Duyarlı)

OLGU 5.

Komplikasyon	YOK	DİYABETİK AYAK YARASI			
Yatırılış Nedeni	AMELİYAT	**Yatış Çıkış Tarihleri**	06.07.2015	**Dosya No**	
TANI	E11.2 - geç yetişkin-başlangıçlı, diabetes (mellitus) (obes olmayan) (obes) (Kesin Tanı) E13.5 - Diyabetes mellitüs, diğer tanımlanmış, periferik dolaşım komplikasyonuyla birlikte (Kesin Tanı) E78.2 - Hiperlipidemi karma (Kesin Tanı) N18.8 - Kronik böbrek yetmezlikleri, diğer (Kesin Tanı) S91.2 - Tırnağın etkilendiği ayak parmak(lar)ın açık yarası (Birincil Tanı) (Kesin Tanı) S91.3 - Ayağın diğer kısımlarının açık yarası (Kesin Tanı)				
ŞİKAYET : SAĞ TOPUKTA AÇIK YARA					
HİKAYE : 9 YILDIR TİP 1 DM HASTASI OLUP 9 YILDIR İNSÜLİN KULLANAN HASTANIN YAKLAŞIK2 YIL ÖNCE SAĞ TOPUKTA PARAKERATOTİK KANAMALI LEZYON ŞEKLİNDE BAŞLAYAN AÇIK YARASI İLERLEYEREK TOPUK BOYUNCA KURU NEKROZA DÖNÜŞMÜŞ. HASTAYA BÖBREK YETMEZLİĞİ NEDENİYLE DIŞ MERKEZDE BÖBREK TRANSPLANTASYONU UYGULANMIŞ VE AÇIK YARASININ DEĞERLENDİRİLMESİ İÇİN TARAFIMIZA YÖNLENDİRİLMİŞ. SİLVERDİNLE PANSUMANLA YARASI TAKİP EDİLEN HASTA YAKLAŞIK 16 AY ÖNCE KLİNİĞİMİZE DEBRİDMAN AMAÇLI YATIRILMIŞ. 12 AY ÖNCE YARA KAPANMAMASI SEBEBİYLE ANKARA´DA 4 FARKLI HASTANEDE MUAYENE OLAN HASTA 07.07.2014 TARİHİNDE CTF PLASTİK, REKONSTRUKTİF VE ESTETİK CERRAHİ POLİKLİNİĞİNDE MUAYENE EDİLMİŞ VE ENFEKSİYON HASTALIKLARI TAKİBİ ÖNERİLMİŞ. 08.07.2014´DE CTF ENFEKSİYON HASTALIKLARI BİRİMİ´NE TETKİK VE TEDAVİ AMAÇLI YATIŞI OLAN HASTANDA AYAKTA AÇIK YARA VE OSTEOMYELİT TANISI KONMUŞ, 18.07.2014´DE A.B TEDAVİSİ İLE TABURCU EDİLMİŞ. HASTA 18.07.2014 TARİHİNDE TETKİK VE TEDAVİ AMAÇLI CTF PLASTİK CERRAHİ SERVİSİNE YATIRILDI. PANSUMAN İLE TAKİP SONRASI TABURCULUĞU YAPILAN HASTA AYAKTAN TAKİBİNDE AÇIK YARANIN KAPANMAMASI NEDENİYLE BİRİMİMİZE 2. KEZ BAŞVURDU VE OPERE EDİLMEK ÜZERE YATIRILDI. DEBRİDMAN + GREFT UYGULANAN VE TABURCU EDİLEN HASTANIN GREFTİNDE TOTAL KAYIP OLMASI ÜZERİNE MAYIS AYINDA SERVİSİMİZE YATIRILAN HASTAYA DEBRİDMA+ SERBEST DOKU AKTARIMI UYGULANMIŞ. HASTANIN FLEP ALTINDA YAŞ NEKTORİTK YARASI GELİŞMESİ ÜZERİNE TEDAVİ AMAÇLI SERVİSİMİZE YATIRILDI.				
ÖZGEÇMİŞ : HT,HİPERKOLESTEROLEMİ,TİP 1 DM, BÖBREK TRANSPLANTASYONU					
SOYGEÇMİŞ : AĞABEYİ 2 YIL ÖNCE SVO NEDENİ İLE EXİTUS					
GEÇİRDİĞİ HASTALIKLAR : BÖBREK YETMEZLİĞİ					

OLGU 5.

Protokol		**Kimlik No**	19402110682	**Doğum Tarihi**	15.05.1977
Ad Soyad				**Yaş / Cinsiyet**	38 / E

İstek Tarih	13.07.2015	**İsteyen Birim**	PLASTİK CERRAHİ SERVİSİ A	**İsteyen Doktor**
Konsültasyon Tarih	13.07.2015	**Birim**	ENFEKSİYON HASTALIKLARI KONSÜLTASYON HEKİMLİĞİ	**Doktor**

HASTA BİLGİ : SN MESLEKTAŞIM, HASTANIN YARA KÜLTÜRÜ SONUÇLARI ÇIKMIŞTIR.TARAFINIZCA DEĞERLENDİRİLMESİ RİCA OLUNUR

AÇIKLAMA : HASTA YATAĞINDA DEĞERLENDİRİLDİ GD İYİ ATEŞSİZ VİTALLERİ STABİL
6/7 YARA YERİ KX E.COLİ+ACİNETOBACTER+ MRSA ÜREMESİ VAR
ODAK KONTROLUNUN SAĞLANMASIYLA BİRLİKTE TAZOCİN TED. KESİLİP KÜLTÜR DUYARLILIK SONUCUNA GÖRE SULPEROZON
2*2+TARGOCİD 1*800 YUKLEME DOZUNUN ARDINDAN 1*400 İDAME DOZU BAŞLANMAIS
AKUT FAZ GD TAKIBIYLE GEREĞİNDE REKONS

Sefoperazon /sulbaktam → Kültür negatif → Klinik daha iyi

OLGU 5.

Bir ay sonra → ESBL+ E.coli → Acinetobacter tekrar üremedi → Takiplerinde üreme olmadı

Protokol		**Doğum Tarihi**	15.05.1977
Ad Soyad		**Yaş / Cinsiyet**	38 / E

İstek Tarih	10.08.2015	**İsteyen Birim**	PLASTİK CERRAHİ SERVİSİ A	**İsteyen Doktor**	
Konsültasyon Tarih	10.08.2015	**Birim**	ENFEKSİYON HASTALIKLARI KONSÜLTASYON HEKİMLİĞİ	**Doktor**	
HASTA BİLGİ : YARA KÜLTÜRÜNDE Escherichia coli (Genişletilmiş spektrumlu beta-laktamaz yapan) ÜREMESİ OLAN HATSNAIN TARAFINIZCA DEĞERLENDİRLMESİ RİCA OLUNUR.					
AÇIKLAMA : YARA KÜLTÜRÜNDE ESBL + ÜREMESİ OLAN HASTANIN MEVCUT ANTİBİYOTİKLERİ KESİLEREK ERTAPENEM 1*1 GR İV TEDAVİ BAŞLANMASI VE GEREĞİNDE REKOSN ÖENRİLİR					

Adım adım kolistin direnci...

Clin Lab. 2015;61(7):741-7.

OXA-type Carbapenemases and Susceptibility of Colistin and Tigecycline Among Carbapenem-Resistant Acinetobacter Baumannii Isolates from Patients with Bacteremia in Turkey.

Cakirlar FK, Ciftci IH, Gonullu N.

Abstract

BACKGROUND: Carbapenem-resistant Acinetobacter baumannii (CRAB) has emerged as one of the most troublesome pathogens in healthcare settings worldwide. The present study was conducted to analyze the genes encoding resistance to carbapenems and to determine in vitro activity of colistin and tigecycline against CRAB isolates from blood culture of hospitalized patients at Istanbul University Cerrahpasa Medical School hospital.

METHODS: Between January 2012 and June 2014, a total of 72 CRAB isolates were isolated by conventional methods from blood cultures of patients with bacteremia who were hospitalized in intensive care units and in various departments of the hospital. The isolates were confirmed using a Phoenix automated system. Antibiotic susceptibilities were determined by disk diffusion method and Etest. Molecular detection of resistance genes were screened by multiplex real time polymerase chain reaction (qPCR) and PCR parameters.

RESULTS: CRAB isolates were highly resistant to tetracycline (86.1%), trimethoprim/sulfamethoxazole (84.7%), ceftazidime (83.3%), cefepime (81.9%), ciprofloxacin (81.9%), amikacin (75.0%), piperacillin/tazobactam (75.0%), cefotaxime (72.2%), and gentamicin (69.4%). Tigecycline and colistin resistance were not detected. MIC50 and MIC90 of tigecycline (MIC ranges 0.016-1 µg/mL) and colistin (MIC ranges 0.125-1.5 µg/mL) were found to be 0.5 µg/mL and 1 µg/mL, respectively. All isolates were positive for OXA-51 that shows molecular identification of A. baumannii. Fifty-one (70.8%) and 2 (2.8%) of these isolates were positive for OXA-23 and OXA-58 genes, re- spectively.

CONCLUSIONS: This study indicated the most of the CRAB isolates in our hospital carry the OXA-23 gene. Colistin and tigecycline resistance were not detected. However, significant effort must be done to prevent the spread of OXA-23-producing CRAB-isolates and continuous monitoring of drug resistance is necessary in clinical settings.

CTF 2012-2014 72 KDAB → %100 OXA-51, %70 OXA-23, %3 OXA-58
Kolistin ve TIG direnci Ø → OXA-23 yayılımına dikkat

- İlk karbapenem dirençli A. baumannii (KDAB) → 1991
- İlk karbapenem hidrolize eden oksasilinaz → → Oxa 23→ 1995
- İlk KDAB salgını → ABD, 1991

Kuo et al., 2004
Scaife et al., 1995
Go et al., 1994


KARBAPENEMAZLAR
SINIF A
SME, NMC, IMI, GES, KPC
SINIF B
METALLOBETALAKTAMAZLAR (GIM, IMP, SPM, SIM, VIM) ve (NDM-1)
SINIF C
Amp C
SINIF D
Oxasilinazlar

OXA-51 = A. baumannii

JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 2006, p. 2974–2976 Vol. 44, No. 8
0095-1137/06/$08.00+0 doi:10.1128/JCM.01021-06

Identification of *Acinetobacter baumannii* by Detection of the *bla*$_{\text{OXA-51-like}}$ Carbapenemase Gene Intrinsic to This Species

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Received 16 May 2006/Returned for modification 6 June 2006/Accepted 8 June 2006

***bla*$_{\text{OXA-51-like}}$ was sought in clinical isolates of *Acinetobacter* species in a multiplex PCR, which also detects *bla*$_{\text{OXA-23-like}}$ and class 1 integrase genes. All isolates that gave a band for *bla*$_{\text{OXA-51-like}}$ identified as *A. baumannii*. This gene was detected in each of 141 isolates of *A. baumannii* but not in those of 22 other *Acinetobacter* species.**

Acinetobacter baumannii is an increasingly important nosocomial pathogen that particularly affects critically ill patients. It is associated with multiple antibiotic resistance, and many widespread strains are resistant to almost all antibiotics currently in use (4, 7, 8, 9, 10). There is mounting evidence that *A. baumannii* has a naturally occurring carbapenemase gene intrinsic to this species (5, 11, 13). The first report of this gene described *bla*$_{\text{OXA-51}}$ (2), but since then a large number of closely related variants have been found (with OXA numbers 64, 65, 66, 67, 68, 69, 70, 71, 75, 76, 77, 83, 84, 86, 87, 88, 89, 91, 92, 94, and 95) (1, 5, 11), and we have referred to them collectively as "*bla*$_{\text{OXA-51-like}}$" genes. Carbapenem resistance has only been associated with these genes when the insertion sequence IS*Aba1* is upstream (11) and is not an indicator of whether an isolate has such a gene.

Although it is clear that *bla*$_{\text{OXA-51-like}}$ genes are present in at least the vast majority of isolates of *A. baumannii*, there has been some debate as to whether they are present in all isolates of this species (3). If they are consistently found and are also unique to this species, then their detection could provide a simple and convenient method of identifying *A. baumannii* which could more easily be carried out than current definitive methods, such as amplified rRNA gene restriction analysis (12) (ARDRA), and which would be more reliable than biochem-

Since *A. baumannii* is clinically by far the most significant of the *Acinetobacter* species, the ability to distinguish it rapidly from other members of the genus would be highly valuable.

Here we describe the results of testing large numbers of well-characterized clinical *Acinetobacter* isolates for *bla*$_{\text{OXA-51-like}}$ genes by PCR with group-specific primers (13) and compare the results with those obtained by ARDRA. Detection of *bla*$_{\text{OXA-51-like}}$ can be carried out as part of a multiplex, and two such multiplexes (one detects all the known groups of OXA carbapenemase genes in *Acinetobacter* [13], and the second detects *bla*$_{\text{OXA-51-like}}$, *bla*$_{\text{OXA-23-like}}$, and the class 1 integrase gene) are in current use in our laboratories; the class 1 integrase gene is a useful marker for outbreak strains of *A. baumannii* (6, 10).

All isolates of *Acinetobacter* received by the United Kingdom reference laboratories between November 2005 and March 2006 were included (170 isolates). Every isolate was compared with previous isolates by pulsed-field gel electrophoresis (PFGE) of ApaI-digested DNA, using BioNumerics software, as described previously (9, 10). The set included 64 isolates of OXA-23 clone 1 (the most prevalent genotype in the United Kingdom), 22 isolates of the South East clone, 18 isolates of the T strain, and 1 isolate each of the W strain (known to

OXA-23 klon II

- Avrupa bölgesinde görülen üç major A. baumannii klonundan biri
- Daha virülan, salgın potansiyeli yüksek
- Klon I → Güney Afrika, Çek cumhuriyeti, Polonya, İtalya, İspanya → salgınlar
- Klon II → G Afrika, İspanya, **Türkiye,** Yunanistan, Fransa → salgınlar
- Klon III→ Hollanda, İtalya, Fransa, İspanya

Promedmail

Giamarellou et al., 2008

Van Dessel et al., 2004

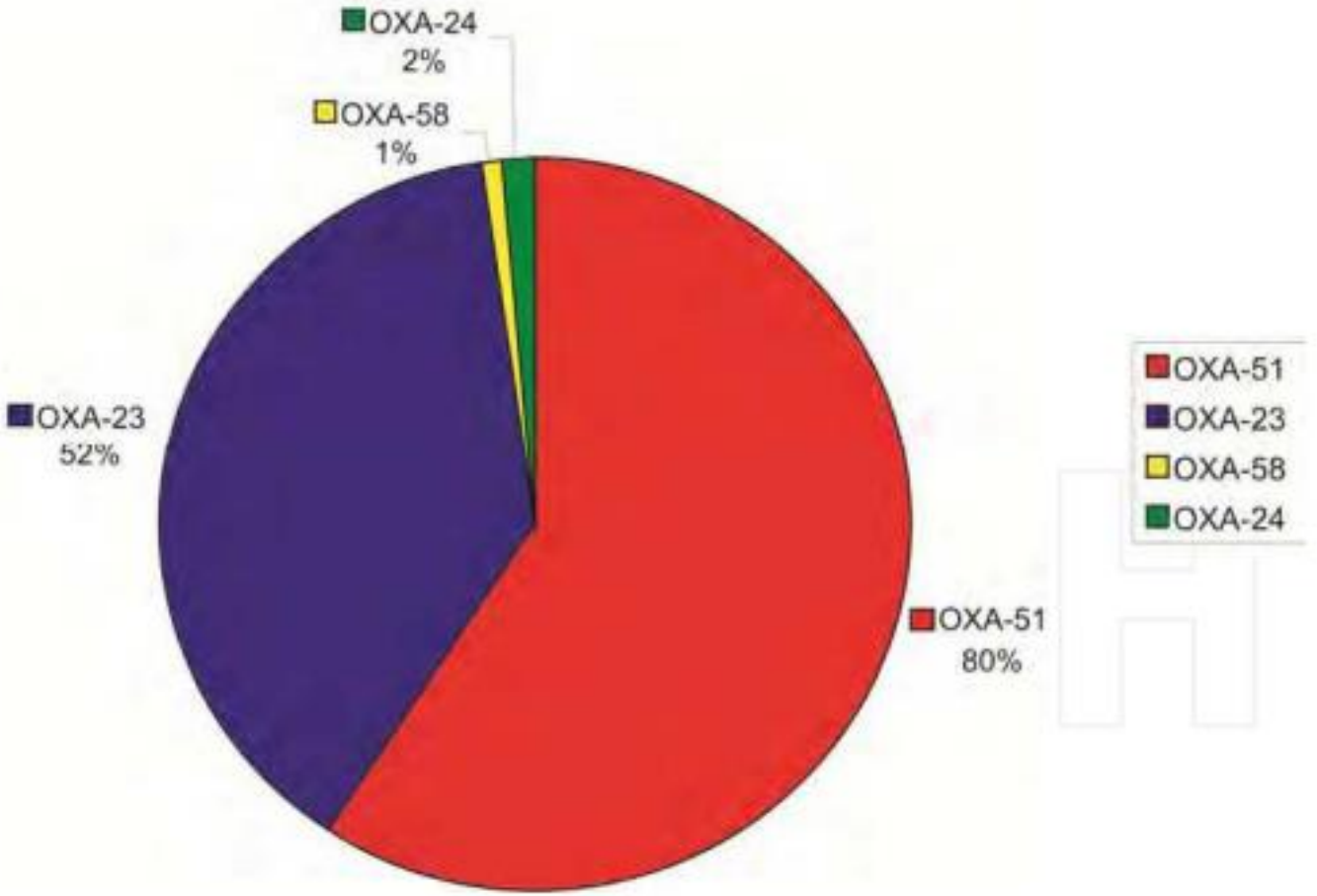


Fig. 4. Pie chart showing the results of the Multiplex PCR I for the prevalence of the OXA genes in the 97 *Acinetobacter baumannii* isolates obtained from a Tertiary Academic Hospital

Klas D karbapenemazların dünya geneli dağılımını temsilen

Feizabadi et al., 2008

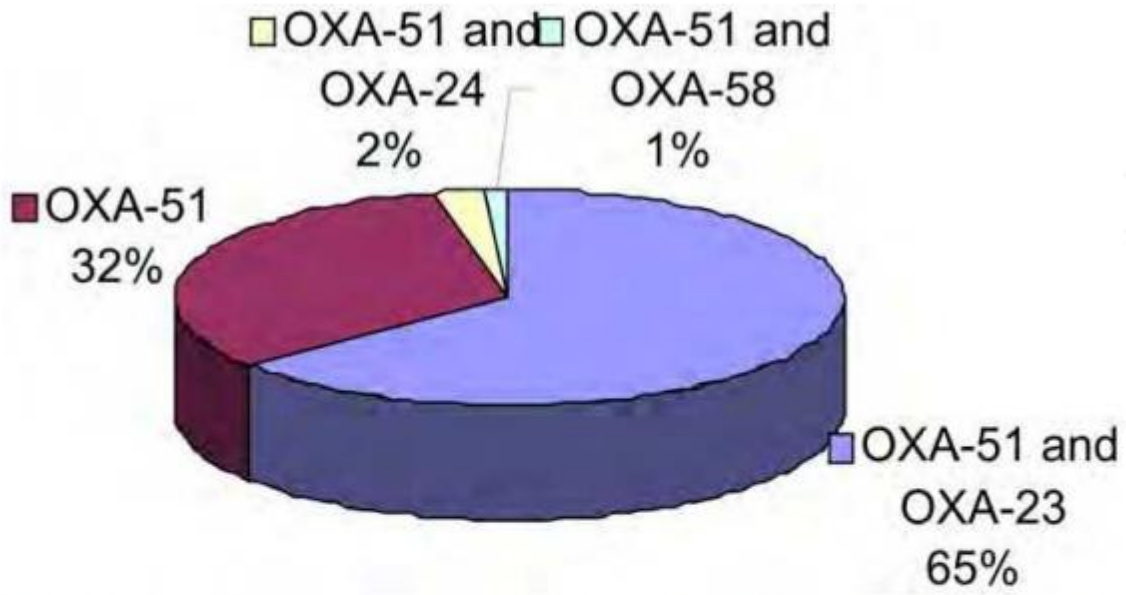
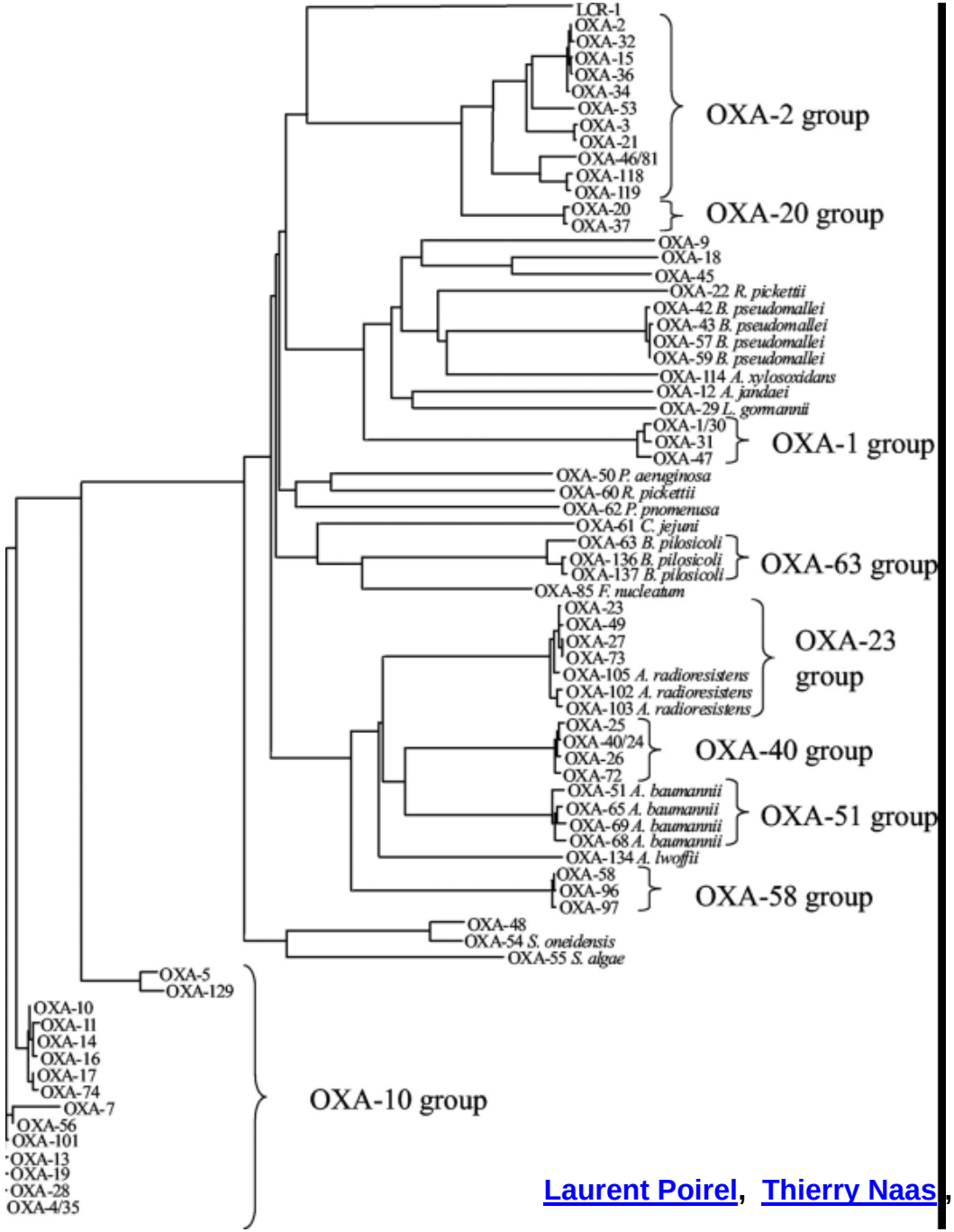


Fig. 6. Pie chart showing the results of the Multiplex PCR I for the four strains of *Acinetobacter baumannii* circulating in a Tertiary Academic Hospital



Yeni gruplar…

OXA-24/40 grup

OXA-25, OXA-26, OXA-72, OXA-160…

OXA 149

Laurent Poirel, Thierry Naas, Patrice Nordmann* AAC 2010

J Antimicrob Chemother. 2006 Sep;58(3):537-42. Epub 2006 Jul 1.

High prevalence of OXA-51-type class D beta-lactamases among ceftazidime-resistant clinical isolates of Acinetobacter spp.: co-existence with OXA-58 in multiple centres.

Vahaboglu H[1], Budak F, Kasap M, Gacar G, Torol S, Karadenizli A, Kolayli F, Eroglu C.

⊕ Author information

Abstract

OBJECTIVES: This study was designed to demonstrate the prevalence of the newly discovered carbapenem-hydrolysing class D enzymes, OXA-51-type and OXA-58, among clinical isolates of Acinetobacter spp.

METHODS: A total of 72 isolates from six centres were studied. Isolates were screened by PCR with specific primers for bla(OXA-51-type) and bla(OXA-58). PCR products were sequence-analysed. Plasmids were digested with EcoRV and genomic DNAs were digested with PvuII. Hybridization experiments were done with digoxigenin-labelled specific probes. Macro-restriction analysis was done on SmaI-digested genomic DNAs.

RESULTS: A total of 56 (77.8%) isolates were positive for bla(OXA-51-type) genes. Sequence analysis of the products from 23 selected isolates revealed the occurrence of multiple alleles in all contributing centres. The bla(OXA-58) gene was detected among 10 isolates from five centres. All were also positive for bla(OXA-51-type) genes. Among the bla(OXA-58)-positive isolates, two from the same centre were positive for a novel OXA-51 allele (OXA-86). Southern hybridization of plasmids and of genomic DNAs suggested that bla(OXA-51-type) genes are located on chromosomes whereas bla(OXA-58) genes are plasmid borne in these 10 isolates. Plasmid profiles and pulsed-field gel electrophoresis patterns indicated the spread of the bla(OXA-58) gene among multiple clones. The bla(OXA-51-type) and bla(OXA-58) co-carrier strains were mostly associated with a pandrug-resistant phenotype.

CONCLUSIONS: This study indicated that bla(OXA-58)-bearing plasmids are readily spreading among multiple clones of the bla(OXA-51-type)-bearing clinical isolates of Acinetobacter spp. Since these isolates are highly resistant to antibiotics this finding indicates the existence of a significant problem in Turkish hospitals.

High prevalence of OXA-51-type class D β-lactamases among ceftazidime-resistant clinical isolates of *Acinetobacter* spp.: co-existence with OXA-58 in multiple centres

Table 1
Occurrence of OXA-51-type β-lactamase-positive isolates of *Acinetobacter* spp. in six ICUs

	(1)	(2)	(3)	(4)	(5)	(6)	
OXA-51 alleles	**Istanbul[a]**	**Kocaeli**	**Samsun**	**Trabzon**	**Izmir**	**Kayseri**	**Total**
Positive							
OXA-51	2			2	4		8
OXA-64	1						1
OXA-66			2	2		3	7
OXA-68	1	1			1		3
OXA-69			1		1		2
OXA-86						2	2
NSI[b]	2	1	6	8	3	13	33
Total	6	2	9	12	9	18	56 (77.8%)
Negative	2		6	2	1	5	16
Grand total	8	2	15	14	10	23	72

[a]Names of the cities of contributing centres.

[b]NSI, sequence identification not obtained.

İki önemli bulgu;

1) OXA 51 ve OXA 58 ENZİMLERİ birlikte → Pandrug R
2) Çoğu kökende Tigesiklin MİK'leri >2 → R

Vahaboğlu ve ark, JAC, 2006

Int J Antimicrob Agents. 2010 Aug;36(2):114-8. doi: 10.1016/j.ijantimicag.2010.03.017. Epub 2010 May 26.

Characterisation of carbapenem-resistant Acinetobacter baumannii outbreak strains producing OXA-58 in Turkey.

Kulah C[1], Mooij MJ, Comert F, Aktas E, Celebi G, Ozlu N, Rijnsburger MC, Savelkoul PH.

⊕ Author information

Abstract

The aim of this study was to characterise the molecular epidemiology and mechanisms of carbapenem resistance of nosocomial Acinetobacter baumannii isolates in a new university hospital in Turkey. A total of 145 carbapenem-resistant A. baumannii (CRAB) isolates were collected during the period 2003-2006. All isolates were typed by amplified fragment length polymorphism (AFLP) analysis. AFLP analysis showed three predominant clusters consisting of 72, 20 and 12 clinical strains as well as some smaller clusters and 23 unique strains. The three main clonal AFLP types corresponded to three major antibiotic susceptibility patterns. One environmental isolate was found related to the major outbreak clone. The reference type strains of European clones I, II and III were also typed by AFLP and analysed for clonal similarity. Polymerase chain reaction (PCR) analysis of different carbapenem resistance genes showed that strains from each of the three main clusters as well as 79% of the remaining strains harboured the bla(OXA-58) gene. No genes encoding the metallo-beta-lactamases GIM-1, SIM-1, SPM-1, IMP-like and VIM-like or the oxacillinases OXA-24-like and OXA-23-like were detected. In conclusion, multiple clones of CRAB strains producing OXA-58-type oxacillinase were responsible for a sustained CRAB outbreak occurring in a hospital in Turkey. These isolates were not associated with A. baumannii strains of the major European clones I, II or III.

145 KDAB kökeni → AFLP analizi → 3 büyük küme →hepsi **bla(OXA-58)**
MBL Ø OXA-23 Ø major Avrupa klonlarından (I-II-III) farklı

Infect Genet Evol. 2013 Mar;14:92-7. doi: 10.1016/j.meegid.2012.11.003. Epub 2012 Dec 1.

Clonal diversity and high prevalence of OXA-58 among Acinetobacter baumannii isolates from blood cultures in a tertiary care centre in Turkey.

Metan G[1], Sariguzel F, Sumerkan B, Reijden Tv, Dijkshoorn L.

⊕ Author information

Erratum in
Infect Genet Evol. 2013 Jun;16:447-8.

Abstract

Genotypic diversity, antimicrobial susceptibilty, and presence of OXA-genes were assessed in 100 nosocomial Acinetobacter strains from a tertiary-care hospital, Turkey. Ninety-eight isolates were identified by AFLP library identification to Acinetobacter baumannii. Furthermore, the isolates were divided into 30 AFLP clusters and single strains at a similarity cut-off level of 90%, the defined strain level. Most of these clusters grouped together in larger clusters at a lower similarity level, indicating diversification beyond the strain level. At a similarity level of 80%, the A. baumannii isolates were allocated to eight clusters of multiple isolates (A, C, D, E, G, H, J, L) and 3 single isolates (B, F, I). Comparison of the isolates to those of the Leiden AFLP database revealed that the large cluster H (41 isolates) corresponded to a tentative novel international clone previously identified both by AFLP and MLST (CC15). Clusters D and E grouped with European (EU) clone II isolates, and cluster J with those EU clone I. Clusters A, C, G, and L could not be identified to any international clone. MLST of selected isolates of the major clusters corroborated the clone allocation by AFLP, except for the tested cluster A isolate which was identified to CC2 (EU clone II). Carbapenem resistance of 75 A. baumannii isolates was associated with the blaOXA-58-like gene or blaOXA-51-like with ISAba1 upstream. Altogether, 99% of the Acinetobacter isolates were multidrug resistant (MDR) and 77% extensively drug resistant (XDR). The findings show that multiple strains and clones MDR and XDR A. baumannii were endemic in the hospital.

98 KDAB → 30 AFLP kümesi →%80 benzerlik: 8 küme, 3 tek köken→
İki küme EU klon II, bir küme EU klon I ile gruplandı
%75 bla(OXA-58) veya bla(OXA-51)
%77 XDR

KDAB bakteremilerinde tedavi: Ne verirsen kolistinle...

Eur J Clin Microbiol Infect Dis. 2014 Aug;33(8):1311-22. doi: 10.1007/s10096-014-2070-6. Epub 2014 Feb 15.

Comparison of colistin-carbapenem, colistin-sulbactam, and colistin plus other antibacterial agents for the treatment of extremely drug-resistant Acinetobacter baumannii bloodstream infections.

Batirel A[1], Balkan II, Karabay O, Agalar C, Akalin S, Alici O, Alp E, Altay FA, Altin N, Arslan F, Aslan T, Bekiroglu N, Cesur S, Celik AD, Dogan M, Durdu B, Duygu F, Engin A, Engin DO, Gonen I, Guclu E, Guven T, Hatipoglu CA, Hosoglu S, Karahocagil MK, Kilic AU, Ormen B, Ozdemir D, Ozer S, Oztoprak N, Sezak N, Turhan V, Turker N, Yilmaz H.

Author information

Abstract

The purpose of this investigation was to compare the efficacy of colistin-based therapies in extremely drug-resistant Acinetobacter spp. bloodstream infections (XDR-ABSI). A retrospective study was conducted in 27 tertiary-care centers from January 2009 to August 2012. The primary end-point was 14-day survival, and the secondary end-points were clinical and microbiological outcomes. Thirty-six and 214 patients [102 (47.7%): colistin-carbapenem (CC), 69 (32.2%): colistin-sulbactam (CS), and 43 (20.1%: tigecycline): colistin with other agent (CO)] received colistin monotherapy and colistin-based combinations, respectively. Rates of complete response/cure and 14-day survival were relatively higher, and microbiological eradication was significantly higher in the combination group. Also, the in-hospital mortality rate was significantly lower in the combination group. No significant difference was found in the clinical ($p = 0.97$) and microbiological ($p = 0.92$) outcomes and 14-day survival rates ($p = 0.79$) between the three combination groups. Neither the timing of initial effective treatment nor the presence of any concomitant infection was significant between the three groups ($p > 0.05$) and also for 14-day survival ($p > 0.05$). Higher Pitt bacteremia score (PBS), Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Charlson comorbidity index (CCI), and prolonged hospital and intensive care unit (ICU) stay before XDR-ABSI were significant risk factors for 14-day mortality ($p = 0.02$, $p = 0.0001$, $p = 0.0001$, $p = 0.02$, and $p = 0.01$, respectively). In the multivariable analysis, PBS, age, and duration of ICU stay were independent risk factors for 14-day mortality ($p < 0.0001$, $p < 0.0001$, and $p = 0.001$, respectively). Colistin-based combination therapy resulted in significantly higher microbiological eradication rates, relatively higher cure and 14-day survival rates, and lower in-hospital mortality compared to colistin monotherapy. CC, CS, and CO combinations for XDR-ABSI did not reveal significant differences with respect to 14-day survival and clinical or microbiological outcome before and after propensity score matching (PSM). PBS, age, and length of ICU stay were independent risk factors for 14-day mortality.

Sulbaktam fena değil, Rifampin versek mi?...

Kolistin direnci yayılıyor...

J Med Microbiol. 2015 Sep;64(9):993-7. doi: 10.1099/jmm.0.000127. Epub 2015 Jul 14.

Molecular identification of tigecycline- and colistin-resistant carbapenemase-producing Acinetobacter baumannii from a Greek hospital from 2011 to 2013.

Mavroidi A[1], Likousi S[1], Palla E[1], Katsiari M[2], Roussou Z[1], Maguina A[2], Platsouka ED[1].

⊕ Author information

Abstract

An alarming increase in the resistance rates of tigecycline and colistin among carbapenemase-producing Acinetobacter baumannii recovered from a Greek hospital over a 3-year period (2011-2013) was investigated. The antimicrobial resistance profiles and carbapenemase gene content were determined for a collection of colistin- and/or tigecycline-resistant carbapenemase-producing A. baumannii isolates (n = 42), which were recovered consecutively during the study period. A gradual increase in the incidence of blaOXA-23 producers was observed from 2011 to 2013. A cluster of 21 isolates comprised tigecycline-resistant blaOXA-23 producers displayed a single antimicrobial resistance pattern. The emergence of two blaOXA-23 producers resistant to both tigecycline and colistin was documented. Furthermore, determination of the mechanisms of colistin and tigecycline resistance and molecular typing by the tri-locus sequence typing (3LST) scheme for nine isolates recovered from bloodstream infections were performed. Out of nine isolates, five tigecycline- and two colistin-resistant isolates were blaOXA-23 producers of 3LST ST101 corresponding to the international clone II recovered during 2012-2013. All nine isolates were positive for the presence of the adeB gene of the AdeABC efflux pump. Three colistin-resistant isolates possessed novel substitutions in PmrB, which may be implicated in colistin resistance. To the best of our knowledge, this is the first report of the acquisition of tigecycline and colistin resistance among blaOXA-23-producing A. baumannii of 3LST ST101 in Greece; thus, continuous surveillance and molecular characterization, prudent use of antibiotics and implementation of infection control measures for A. baumannii are urgent.

Table 5

Main mechanisms of acquired antimicrobial resistance in *Acinetobacter baumannii*

Mechanism	Genetic event	Antimicrobials
High-level expressed AmpC cephalosporinase	Chromosomal mutation	Penicillins (with or without beta-lactamase inhibitors), 3GC
High-level expressed OXA-51-like beta-lactamase	Chromosomal mutation (insertion of IS*Aba1* upstream of *bla OXA-51*)	Carbapenems
Other beta-lactamases		
Extended-spectrum beta-lactamases[a]	MGE acquisition	Penicillins, 3GC
Metallo-beta-lactamases[b] (carbapenemases)		Penicillins, 3GC, carbapenems
Oxacillinase-type carbapenemases[3]		Penicillins, carbapenems
Functional loss of porins (impermeability)	Chromosomal mutation	Variable
Altered penicillin-binding proteins	Chromosomal mutation	Variable
Active efflux pumps		
AdeABC	Chromosomal mutation	Beta-lactams (variable), aminoglycosides, fluoroquinolones, tigecycline
AdeM		Aminoglycosides, fluoroquinolones
AdeIJK		Tigecycline
Aminoglycoside-modifying enzymes[d]	MGE acquisition	Aminoglycosides
16S rRNA methylases	MGE acquisition	Aminoglycosides
Topoisomerases modifications	Chromosomal mutation	Fluoroquinolones
Lipid A (LPS) modifications	Chromosomal mutation	Polymyxins

MGE mobile genetic element (plasmid or transposon), *3GC* third-generation cephalosporins.

Most common enzyme types: [a]PER, VEB and GES (TEM, SHV and CTX-M are rare in *A. baumannii*); [b]VIM, SIM, IMP and NDM; [c]OXA-23-, OXA-40-, OXA-58-, OXA-143 and OXA-235-like; [d]AAC(3), AAC(6′) and APH(3′).

Ann Intensive Care

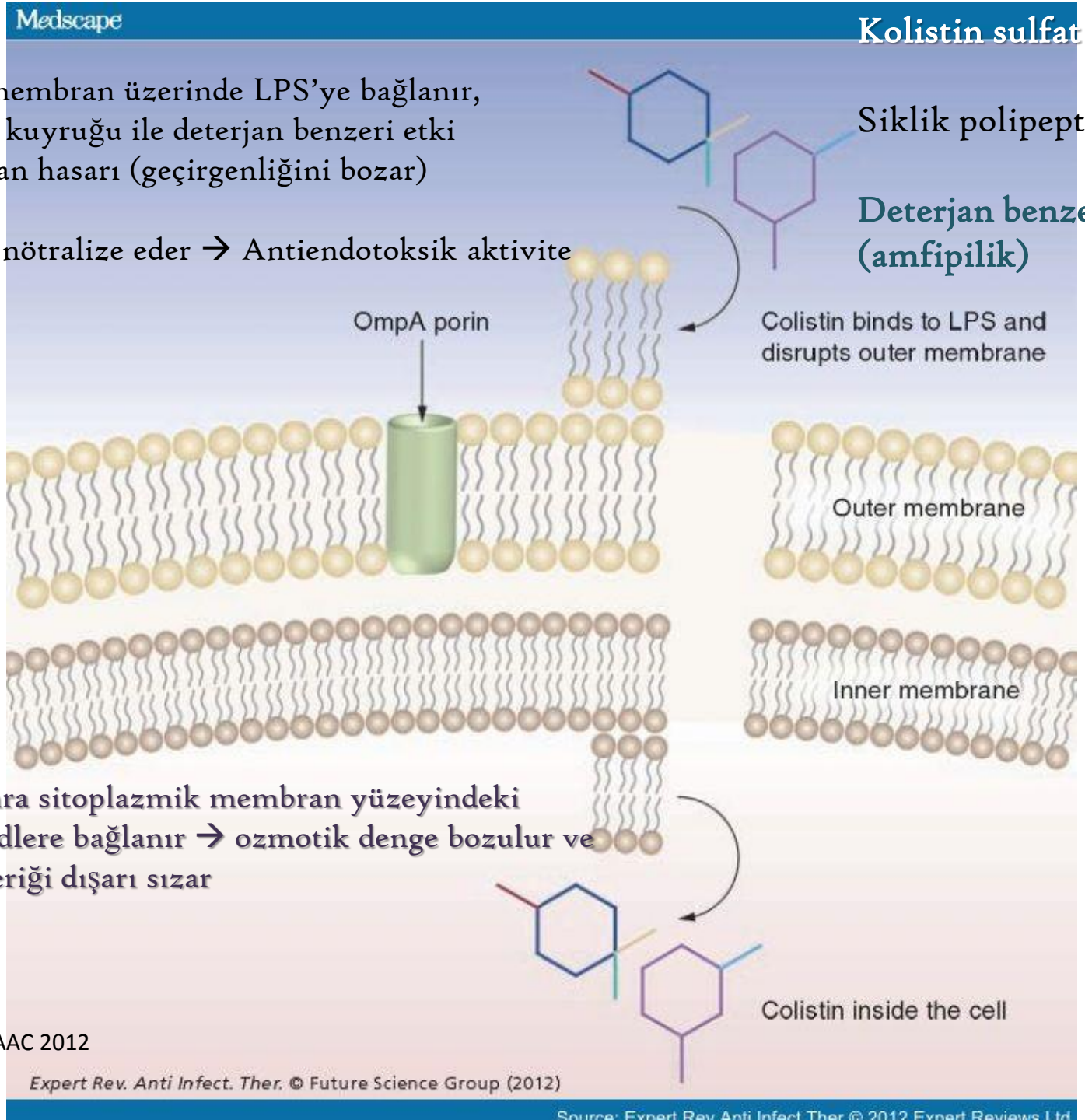
Önce dış membran üzerinde LPS'ye bağlanır, hidrofobik kuyruğu ile deterjan benzeri etki → Membran hasarı (geçirgenliğini bozar)

Lipid A'yı nötralize eder → Antiendotoksik aktivite

Kolistin sulfat

Siklik polipeptid

Deterjan benzeri özellikler (amfipilik)



daha sonra sitoplazmik membran yüzeyindeki fosfolipidlere bağlanır → ozmotik denge bozulur ve hücre içeriği dışarı sızar

Céline Vidaillac, AAC 2012

Kolistin direncinde üç mekanizma:

- (i) Dış membran LPS Lipid A bileşeninin biyosentezini kodlayan genlerin —*lpxA*, *lpxC* or *lpxD*—inaktivasyonu→ Lipid A'nın tam kaybı
- **Lipid A'da modifikasyon** → dış membran net negatif yükünde azalma→ Kolistin afinitesinde azalma
- (ii) Kolistinin proteolitik klivajı
- (iii) Geniş spektrumlu efluks pompasının aktivasyonu

Cai Y, JAC, 2012

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy

Phosphoethanolamine Modification of Lipid A in Colistin-Resistant Variants of *Acinetobacter baumannii* Mediated by the *pmrAB* Two-Component Regulatory System

PowerPoint Slide for Educational Use

(Downloading may take up to 30 seconds. If the slide opens in your browser, select File –> Save As to save it.)

Click on image to view larger version.

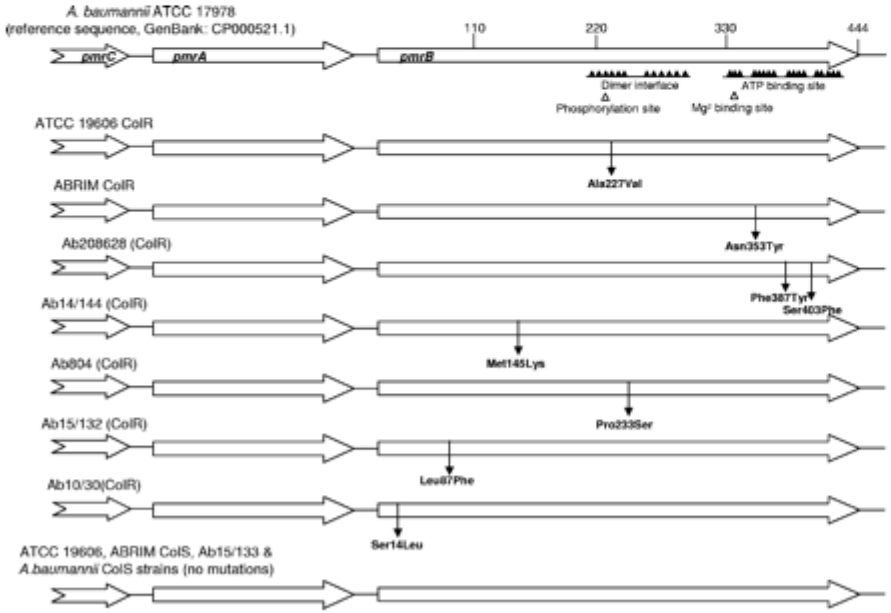


FIG. 1.

Schematic representation of the *pmrCAB* genes. No amino acid changes were

This Article

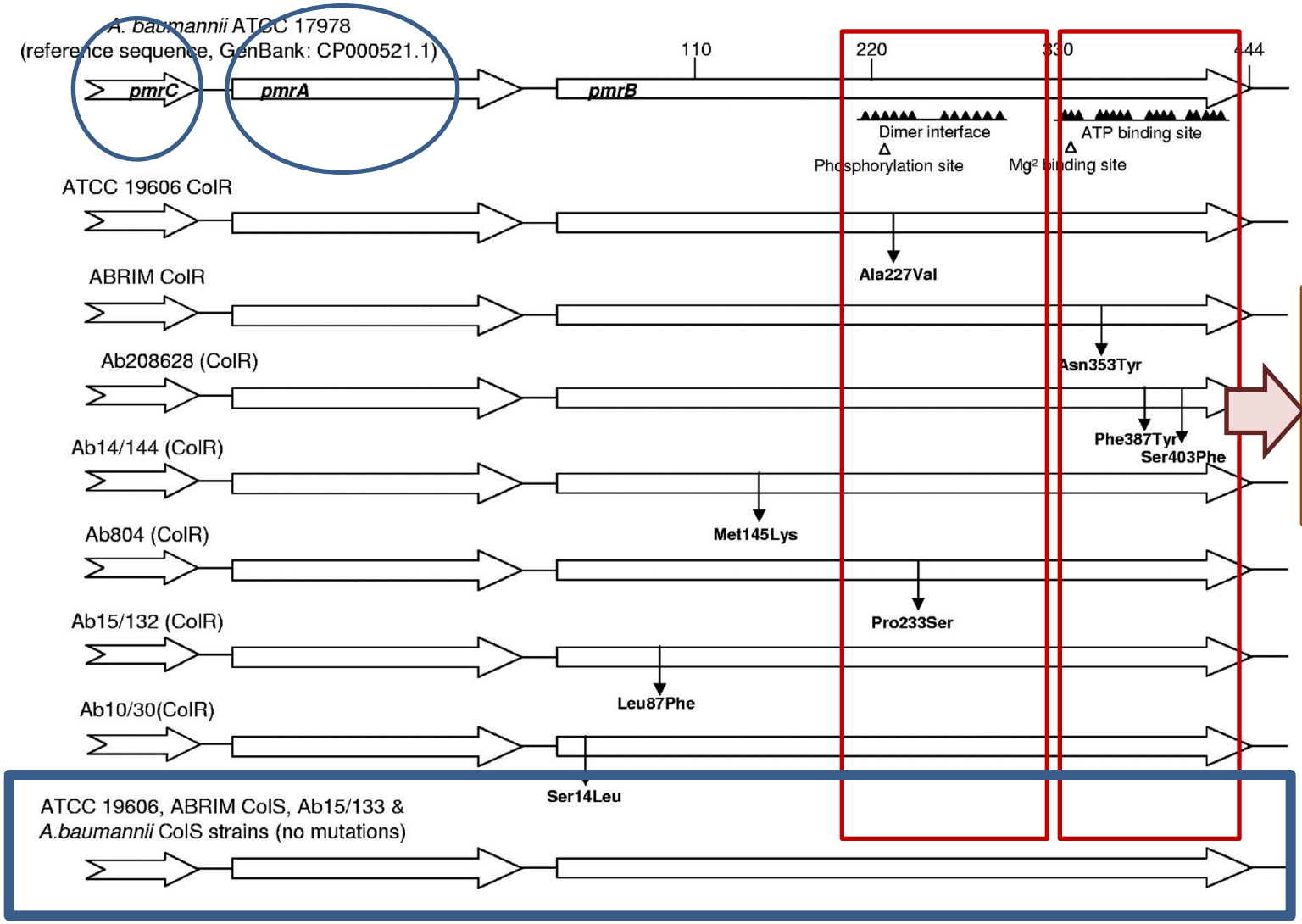
Accepted manuscript posted online May 2011, doi: 10.1128/AAC.00079-11

Antimicrob. Agents Chemother. July 2011 vol. 55 no. 7 3370-3379

Abstract *Free*
Figures
Full Text
PDF

PmrA ve PmrC genlerinde aminoasit değişikliği yok
PmrB'de ise…

Schematic representation of the pmrCAB genes.



"Heptaacylated" Lipid A'ya fosfoetanolamin eklenmesi
→ Kolistin direnci

Alejandro Beceiro et al. Antimicrob. Agents Chemother. 2011;55:3370-3379

Antimicrobial Agents and Chemotherapy

EPİDEMİYOLOJİ

- Çoğu ülkede <%7
- Bulgaristan ve İspanya'dan iki çalışma: %16.7 ve %19.1
- İspanya → %40.7
- Asya'dan bildirilen oranlar : <%12
- Kore: %30.6
- ABD <%2.1
- Güney Amerika: <%7.1
- Heterorezistans→ daha yaygın ancak standart yok, oranlar çok değişken

Ko et al
Cai Y, JAC, 2012

Colistin resistance of *Acinetobacter baumannii*: clinical reports, mechanisms and antimicrobial strategies

Table 1.
Worldwide reports of colistin heteroresistance and resistance of *A. baumannii*

Author (year)	Country/region	Heteroresistance (no. of strains/%)	Resistance (no. of strains/%)
Chang *et al.* (2012)[34]	Taiwan	—	14/10.4
Lee *et al.* (2011)[35]	Taiwan	—	2/9.5
Gales *et al.* (2011)[20]	SENTRY	—	42/0.9
Herrera *et al.* (2011)[13a]	Argentina	14/18.7	0/0
Rolain *et al.* (2011)[21]	France	—	1/—
Al-Sweih *et al.* (2011)[30a]	Kuwait	—	30/12
Lopez-Rojas *et al.* (2011)[22]	Spain		1/—
Keen *et al.* (2010)[38]	USA	—	1/0.1
Rodriguez *et al.* (2010)[14]	Argentina	6/42.9	1/7.1
Rodriguez *et al.* (2009)[15]	Argentina	13/46.4	—
Arroyo *et al.* (2009)[29]	Spain	—	61/40.6
Doi *et al.* (2009)[37]	USA	—	1/—
Eser *et al.* (2009)[31a]	Turkish	—	14/11.3
Gomez-Garces *et al.* (2009)[23a]	Spain	—	1/1.2
Lee *et al.* (2009)[32]	Taiwan	—	2/1.1
Yau *et al.* (2009)[16]	SENTRY	7/23.3	1/3.3
Hawley *et al.* (2008)[18a]	USA	21/100	—
Mezzatesta *et al.* (2008)[24]	Italy	—	1/0.9
Hawley *et al.* (2007)[39a]	USA	—	3/2.1
Quinteira *et al.* (2007)[25]	Portugal	—	10/6.7
Ko *et al.* (2007)[36]	Korea	—	66/30.6
Sung *et al.* (2007)[33]	Korea	—	5/9.1
Li *et al.* (2006)[12]	Australia	15/93.6	—
Dobrewski *et al.* (2006)[27]	Bulgaria	—	3/16.7
Garcia-Penuela *et al.* (2006)[26]	Hong Kong	—	1/3.34
Garcia-Penuela *et al.* (2006)[26]	Spain	—	1/1.36
Tognim *et al.* (2006)[40a]	Brazil	—	2/3
Arroyo *et al.* (2005)[28]	Spain	—	22/19.1
Gales *et al.* (2001)[19a]	SENTRY	—	2/3.3
Hejnar *et al.* (1999)[11a]	Czech Republic	—	5/5.9

[a]*Acinetobacter* spp., including *A. baumannii*.

Yun Cai et al. JAC , 2012 Colistin resistance of *Acinetobacter baumannii*: clinical reports, mechanisms and antimicrobial strategies

TEDAVİ

Kolistin Direncine karşı Antimikrobiyal Stratejiler

Direncin nedeni yetersiz kolistin dozu ?

→Mutant engelleyici konsantrasyon (MEK) çalışmaları bu tezi doğruluyor.

→Test edilen kökenlerin %90'ında MEK >128 mg/L

→günlük dozlar ile bu düzeye çıkılamaz

Düşük doz kolistin, dirençli mutant subpopülasyonları çoğaltıyor.

Kolistin tek başına → q12h, q8h, 24h sürekli infüzyon→ nasıl verilirse verilsin ilk birkaç saat hızla bakterisidal, sonra yeniden üreme başlıyor.

Kolistin yarı ömrü mutad doz aralığından uzun → **doz aralığı çok önemli değil**

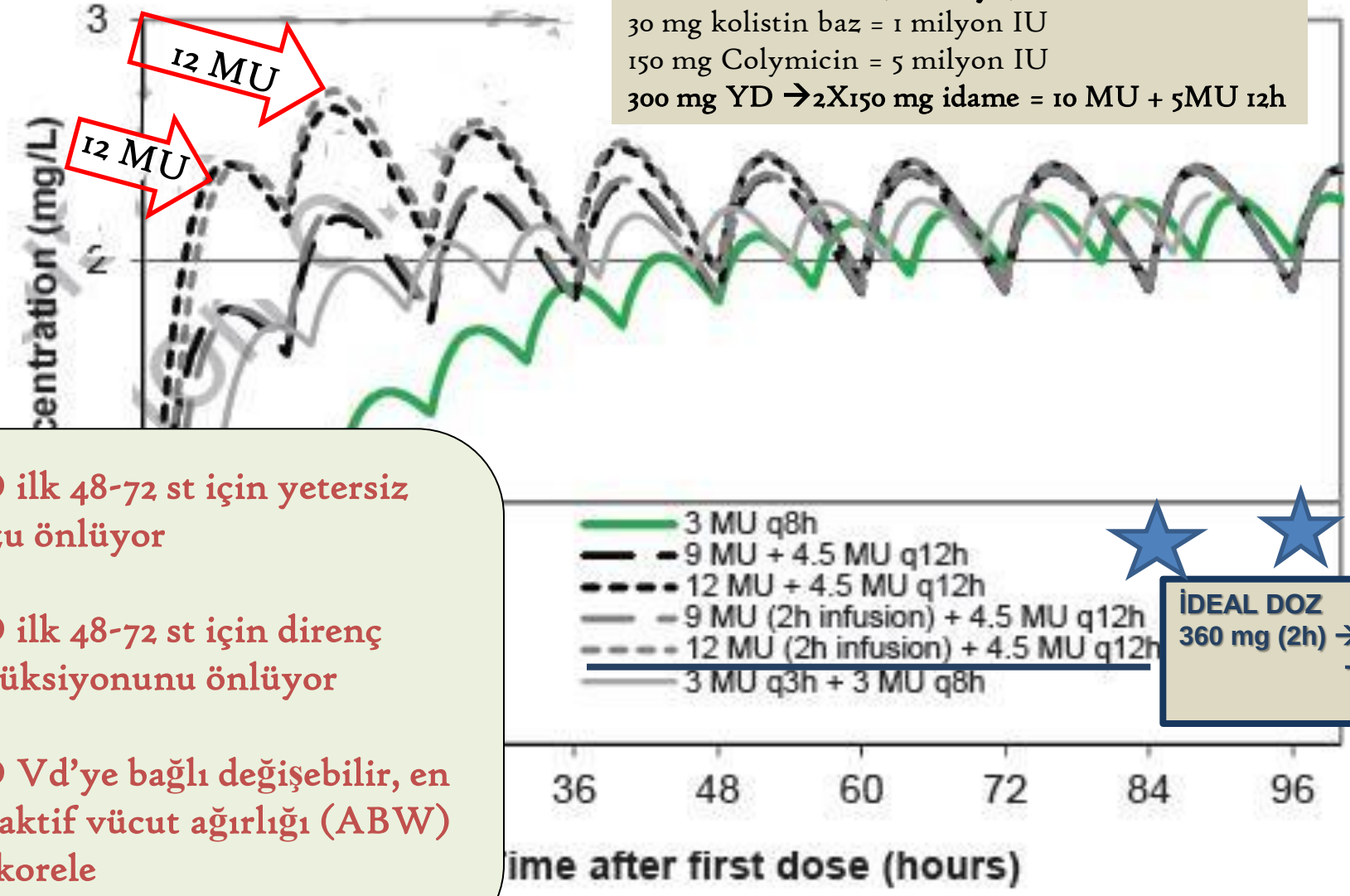
Yükleme dozu ve kombine tedavi ile etkinlik artıyor

Kolistin MİK > 0.5 mg/L ise (ve Krkl>70 mL/min/1.73 m^2) **ise etkin bir ilaçla kombine olarak verilmelidir**

Cai Y, AAC, 2010
Tan CH, AAC, 2007
Plachouras D, AAC, 2009
Garonzik, AAC, 2011

Kolistin farmakokinetiği – Yükleme dozunun önemi

Doz Dönüşümü (Türkiye)
30 mg kolistin baz = 1 milyon IU
150 mg Colymicin = 5 milyon IU
300 mg YD →2X150 mg idame = 10 MU + 5MU 12h



İDEAL DOZ
360 mg (2h) →2x150 mg
→3x100 mg

YD ilk 48-72 st için yetersiz dozu önlüyor

YD ilk 48-72 st için direnç indüksiyonunu önlüyor

YD Vd'ye bağlı değişebilir, en iyi aktif vücut ağırlığı (ABW) ile korele

Plachouras, AAC 2009

Kolistin Uygularken :

- İlacı uygulamadan hemen önce hazırlayın (sulandırıldıktan sonra oda sıcaklığında inaktif forma dönüşüyor)
- Sulandırılan ilaçları bekletmeyin (amfipiliktir → polikatyon ve yağ asitleri → Şişeye yapışıyor)
- Yeterli yükleme dozu verdiniz mi? (300 yerine 375 mg – 2.5 flakon)
- Yeterli idame dozu ayarladınız mı? 2x150 veya 3x100 mg
- TDM olanağınız var mı→ Özellikle zor olgularda (CRRT, yanık, kapiler kaçak vd)
  - Doğru örnekleme ve saklama
  - Sadece valide edilmiş mikrobiyoloji-dışı testler
- Özellikli hasta grupları için ileri araştırmalar gerek
- Hepatobiliyer atılımın önemi henüz tam bilinmiyor

SİNERJİK ETKİLİ KOLİSTİN KOMBİNASYONLARI

in vitro ve *in vivo* çok sayıda çalışma→ Çoğu kolistin duyarlı kökenler ile ilgili

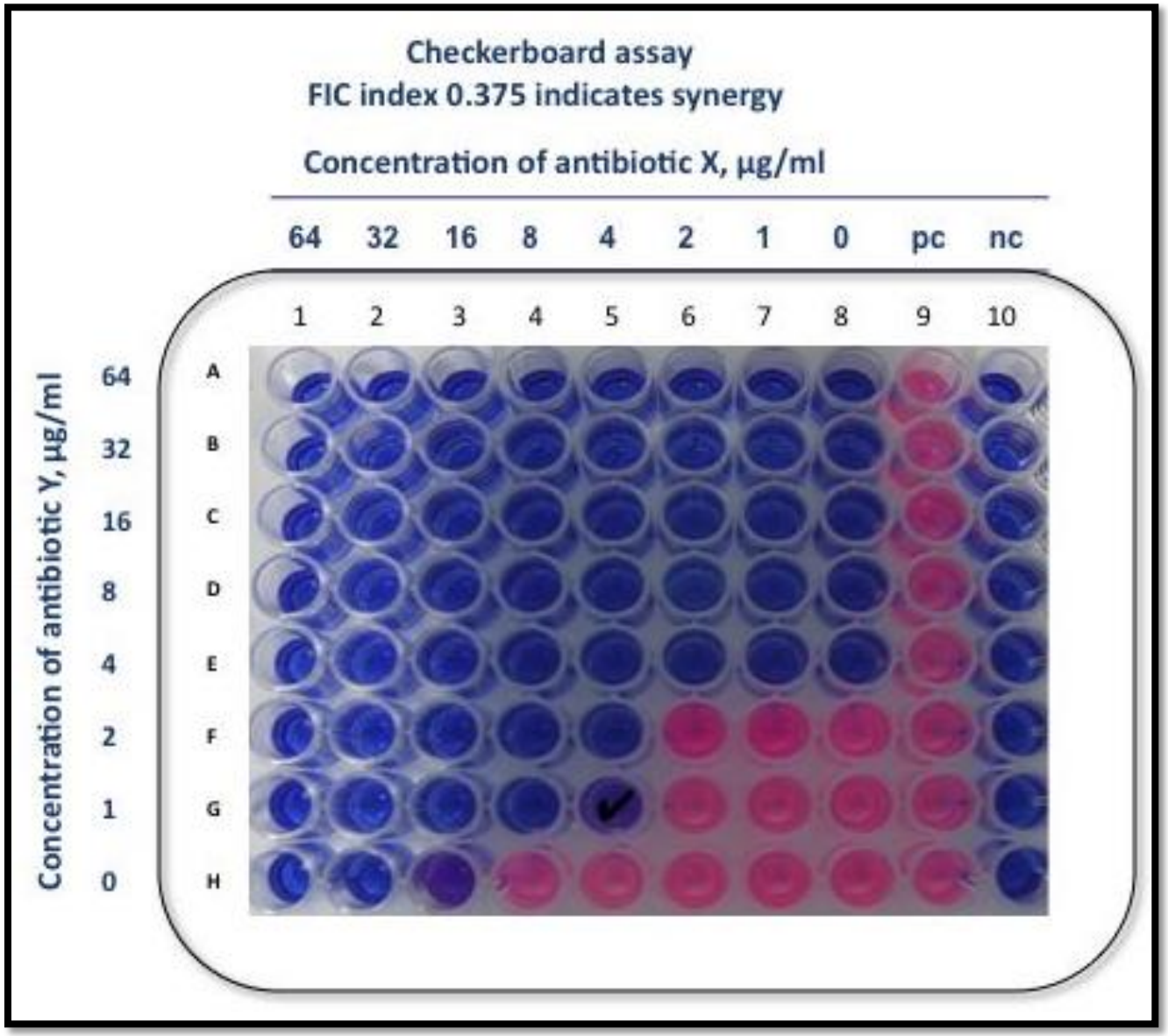
En çok çalışılan kombinasyon → **Kolistin + Rifampin**
→heteroresistansı ve kolistin dirençli mutant gelişimini **ÖNLÜYOR**

Kolistin/imipenem kombinasyonu → heteroresistan A. *baumannii kökenlerine karşı sinerjik (kol/meropenem de öyle 49/52)*

Kolistin/tigesiklin kombinasyonu → iyi sonuçlar

Kolistin / amikasin, Kolistin / fosfomisin, Kolistin /azitromisin → iyi sonuçlar

Rodriguez CH, J Infect Dev Ctries 2010
Principe L, Ann Clin Microbiol Antimicrob 2009
Pankuch GA, AAC, 2008
Timurkaynak F, IJAA, 2006
Fulnecky EJ j Infect 2005
Santimaleeworagun W Southeast Asian J Trop Med Public Health2011



http://www.ibg.kit.edu/nmr/247.php

Fraksiyone İnhibitör Konsantrasyon İndeksi (FİKİ)

FİKA =Kombinasyonda A ilacının MİK'i / A ilacının tek başına MİK'i
FİKB = Kombinasyonda B ilacının MİK'i / B ilacının tek başına MİK'i

FİKİ=FİKA+FİKB

FİKİ ≤0.5→ Sinerjik Etki
0.5- 4→Aditif/farksız Etki
≥4 →Antagonist Etki

Int J Antimicrob Agents. 2006 Mar;27(3):224-8. Epub 2006 Feb 7.

In vitro activities of non-traditional antimicrobials alone or in combination against multidrug-resistant strains of Pseudomonas aeruginosa and Acinetobacter baumannii isolated from intensive care units.

Timurkaynak F[1], Can F, Azap OK, Demirbilek M, Arslan H, Karaman SO.

Author information

Abstract

The aim of this study was to assess the in vitro activity of a number of non-traditional antibiotics (colistin, azithromycin, doxycycline and rifampicin) against multidrug-resistant (MDR) strains of Pseudomonas aeruginosa and Acinetobacter baumannii isolated from Intensive Care Units (ICUs). We also used the checkerboard method to determine whether combinations of colistin with another non-traditional antibiotic or meropenem act synergistically against these strains. Thirty-five P. aeruginosa and 25 A. baumannii strains that were found to be MDR were included the study. Isolates were collected from the specimens of patients in ICUs from 2001 to 2003. All isolates were identified by standard methods and stored at -20 degrees C until use. Antibiotic powders of azithromycin, doxycycline, rifampicin, meropenem and colistin were obtained from their manufacturers. Minimum inhibitory concentrations (MICs) were determined by the agar dilution method on Mueller-Hinton agar. Five strains of A. baumannii and five strains of P. aeruginosa, all of which had different MIC values for colistin, were selected for the synergy study using the checkerboard titration method. The susceptibility results for doxycycline and meropenem were interpreted according to National Committee for Clinical Laboratory Standards guidelines. The susceptibility breakpoints for colistin and rifampicin were established as 4 mg/L and 2 mg/L, respectively, based on previous studies. Pseudomonas aeruginosa ATCC 27853 and Escherichia coli ATCC 25922 were used as control strains. Testing against the P. aeruginosa strains revealed high MIC50 values for all the drugs except colistin. Doxycycline and colistin were both effective against the A. baumannii strains, with high susceptibility rates of 92% and 100%, respectively. Azithromycin had a high MIC50 value against these strains, whilst rifampicin had a moderate effect (susceptibility rate 64%). The combination of colistin and rifampicin was fully synergistic against four A. baumannii and two P. aeruginosa strains. Combinations of colistin with meropenem and of colistin with azithromycin each showed synergistic activity against three A. baumannii isolates, whilst the same combinations resulted in generally additive or indifferent effects against P. aeruginosa strains. The colistin and doxycycline combination was generally partially synergistic or additive against all the isolates. MDR strains of P. aeruginosa and A. baumannii, which cause nosocomial infections with an increasing ratio in recent years, have limited treatment options. According to our in vitro study results, non-traditional antibiotics such as doxycycline and colistin can be an alternative for the treatment of infections caused by these strains. Combinations of colistin with non-traditional antibiotics or meropenem could be promising alternatives for the treatment of infections due to MDR strains of A. baumannii and P. aeruginosa.

Kolistini sıradışı antibiyotiklerle veya meropenemle kombine edebilirsiniz

Research Paper

Synergistic effects of sulbactam in multi-drug-resistant *Acinetobacter baumannii*

Fatih Temocin, Fatma Sebnem Erdinc, Necla Tulek, Meryem Demirelli, Gunay Ertem, Sami Kinikli, Eda Koksal

Infectious Diseases and Clinical Microbiology, Ankara Training and Research Hospital, Ankara, Turkey.

Submitted: February 3, 2014; Approved: May 2, 2015.

Abstract

Acinetobacter baumannii is a frequently isolated etiologic agent of nosocomial infections, especially in intensive care units. With the increase in multi-drug resistance of *A. baumannii* isolates, finding appropriate treatment alternatives for infections caused by these bacteria has become more difficult, and available alternate treatments include the use of older antibiotics such as colistin or a combination of antibiotics. The current study aimed to evaluate the in vitro efficacy of various antibiotic combinations against multi-drug resistant *A. baumannii* strains. Thirty multi-drug and carbapenem resistant *A. baumannii* strains isolated at the Ankara Training and Research Hospital between June 2011 and June 2012 were used in the study. Antibiotic susceptibility tests and species-level identification were performed using conventional methods and the VITEK 2 system. The effects of meropenem, ciprofloxacin, amikacin, tigecycline, and colistin alone and in combination with sulbactam against the isolates were studied using Etest (bioMérieux) in Mueller-Hinton agar medium. Fractional inhibitory concentration index (FIC) was used to determine the efficacy of the various combinations. While all combinations showed a predominant indifferent effect, a synergistic effect was also observed in 4 of the 5 combinations. Synergy was demonstrated in 43% of the isolates with the meropenem-sulbactam combination, in 27% of the isolates with tigecycline-sulbactam, and in 17% of the isolates with colistin-sulbactam and amikacin-sulbactam. No synergy was detected with the sulbactam-ciprofloxacin combination and antagonism was detected only in the sulbactam-colistin combination (6.66% of the isolates). Antibiotic combinations can be used as an alternative treatment approach in multi-drug resistant *A. baumannii* infections.

Key words: acinetobacter, antimicrobial drugs, drug resistance, drug synergism.

Sulbaktam ile Antagonizm!

Kolistin + Glikopeptid sinerjisi

Checkerboard → fraksiyone inhibitör konsantrasyonlar **(FİKler) <0.5**
Letal dozda A. baumannii ile enfekte edilen caterpillar (tırtıl) deneyleri → **monoterapiye kıyasla anlamlı sağkalım *P*<0.05**

Kolistin dış membranı parçalar→ glikopeptid bakteri hücresine girer

Kolistin dirençli Acinetobacter baumannii kökenlerinde vanko/teiko MİKleri kolistin duyarlı kökenlere göre belirgin düşük
[Kol R → sinerji daha güçlü!]

Gordon NC, AAC, 2010
Li J CID 2007

J Antimicrob Chemother. 2011 May;66(5):1047-51. doi: 10.1093/jac/dkr069. Epub 2011 Mar 8.

In vitro activity of teicoplanin combined with colistin versus multidrug-resistant strains of Acinetobacter baumannii.

Wareham DW[1], Gordon NC, Hornsey M.

Author information

Abstract

OBJECTIVES: Antimicrobial treatment of multidrug-resistant Acinetobacter baumannii (MDRAB) remains an important therapeutic challenge. With isolates resistant to all conventional agents now reported, clinicians are increasingly forced to turn to unorthodox combination treatments in the hope that these may be efficacious. Although a potent interaction between vancomycin and colistin has been demonstrated, there are concerns regarding the inherent toxicity of combining these agents in clinical practice. As teicoplanin has less nephrotoxic potential than vancomycin, we assessed whether a colistin/teicoplanin combination would have similar antimicrobial activities in vitro.

METHODS: The antimicrobial activity of colistin alone and in combination with teicoplanin was assessed versus a collection of MDRAB belonging to a number of epidemic lineages present in the UK. Synergy studies were undertaken using microtitre plate chequerboard assays, an Etest agar dilution method and standard time-kill methodology.

RESULTS: The combination of teicoplanin and colistin was bactericidal versus all of the strains tested. In chequerboard assays, fractional inhibitory concentration indices of <0.5 were obtained, consistent with significant in vitro synergy. Using the Etest method the MIC of teicoplanin fell from >256 mg/L to ≤2 mg/L in the presence of subinhibitory concentrations of colistin.

CONCLUSIONS: Significant synergy was observed when colistin was combined with teicoplanin versus MDRAB in vitro. This may represent a useful therapeutic combination for the treatment of A. baumannii infections, especially when renal toxicity is a significant concern.

PMID: 21393131 [PubMed - indexed for MEDLINE] Free full text

Kolistin ile teikoplanin kombinasyonu sinerjik

XDR Acinetobacter'de KOL+RIF, KOL+IPM, IMP+SULB, IPM+RIF

Ann Lab Med. 2016 Mar;36(2):138-44. doi: 10.3343/alm.2016.36.2.138.

In Vitro Synergistic Effects of Antimicrobial Combinations on Extensively Drug-Resistant Pseudomonas aeruginosa and Acinetobacter baumannii Isolates.

Lee H[1], Roh KH[2], Hong SG[3], Shin HB[4], Jeong SH[5], Song W[6], Uh Y[7], Yong D[8], Lee K[9].

⊕ Author information

Abstract

BACKGROUND: Extensively drug-resistant (XDR) Pseudomonas aeruginosa and Acinetobacter baumannii are a threat to hospitalized patients. We evaluated the effects of antimicrobial combinations on XDR P. aeruginosa and A. baumannii isolates.

METHODS: P. aeruginosa and A. baumannii isolates, which were resistant to all antibiotics except colistin (CL), were collected from eight hospitals in Korea. Genes encoding metallo-β-lactamases (MBLs) and OXA carbapenemases were detected by PCR in eight P. aeruginosa and 30 A. baumannii isolates. In vitro synergy of antimicrobial combinations was tested by using the checkerboard method.

RESULTS: Minimum inhibitory concentrations of β-lactams, aminoglycosides, and fluoroquinolones were very high, while that of CL was low for majority of XDR P. aeruginosa and A. baumannii isolates. Antimicrobial combinations including Imipenem (IPM)-CL, ceftazidime (CAZ)-CL, and rifampin (RIF)-CL exerted only additive/indifferent effects on majority of XDR P. aeruginosa isolates. Proportions of XDR A. baumannii isolates that showed synergistic and additive/indifferent inhibition after treatment with antimicrobial combinations used are as follows: IPM-ampicillin-sulbactam (AMS), 17% and 80% isolates, respectively; IPM-rifampin (RIF), 13% and 81% isolates, respectively; IPM-CL, 13% and 87% isolates, respectively; and RIF-COL, 20% and 73% isolates, respectively. Significant proportion (19%) of XDR P. aeruginosa isolates produced MBLs, and majority (82%) of A. baumannii isolates produced either MBLs or OXA-23.

CONCLUSIONS: Our results suggest that combinations of IPM-AMS, IPM-RIF, IPM-CL, and RIF-CL are more useful than individual drugs for treating 13-20% of XDR A. baumannii infections.

KEYWORDS: Acinetobacter baumannii; Combination chemotherapy; In vitro synergy; Pseudomonas aeruginosa

Table 4. Concentrations of antibiotic combinations that exerted synergistic effects on extensively drug-resistant *A. baumannii* isolates

Combination (N of isolates tested)	Strain No.	MICs of individual antimicrobials (μg/mL)		MICs in combination (μg/mL)		Effect of combination
Imipenem-Colistin (4)		Imipenem	Colistin	Imipenem	Colistin	FICI
	9	32	2	4	1	0.375
	11	16	2	4	1	0.5
	25	32	0.5	8	0.12	0.5
	26	64	4	8	0.5	0.25
Imipenem-Ampicillin-Sulbactam (6)		Imipenem	Ampicillin-Sulbactam	Imipenem	Ampicillin-Sulbactam	FICI
	19	32	64	8	16	0.5
	25	32	>128	8	32	0.5
	27	32	8	8	1	0.375
	28	8	4	2	1	0.5
	29	16	4	4	1	0.5
	30	64	8	16	2	0.5
Imipenem-Rifampin (4)		Imipenem	Rifampin	Imipenem	Rifampin	FICI
	12	64	32	16	8	0.5
	25	32	4	8	0.5	0.375
	28	16	8	4	2	0.5
	29	16	4	1	1	0.3125
Rifampin-Colistin (6)		Rifampin	Colistin	Rifampin	Colistin	FICI
	2	4	0.5	1	0.12	0.5
	9	32	2	1	0.5	0.156
	11	32	1	8	0.25	0.5
	25	4	0.5	1	0.12	0.5
	26	64	2	8	0.5	0.375
	29	4	0.5	0.5	0.12	0.375

Sinerjik etki →

(IPM, AMS ve RIF) MİK düzeyleri "dirençli"den → "duyarlı"ya gerilemiştir

Kolistin MİK'i kombine kullanıldığında 2-8 kat düşmüştür

Sonuç: Sinerjik etki varsa invitro tek başına dirençli görünen antibiyotikler kombine olmak koşuluyla tedavide kullanılabilir

İnvitro sonuçlar invivo sinerjiyi göstermeyebilir, klinik çalışmalarla valide edilmelidir

Colistin resistance of *Acinetobacter baumannii*: clinical reports, mechanisms and antimicrobial strategies

Table 2.
Reports of colistin combination therapy to *A. baumannii*

Author (year)	Antibiotic combination	Type of research	Type of AB	Findings
Peck *et al.* (2012)[59]	imipenem or rifampicin or tigecycline	*in vitro*	imipenem-resistant AB, colistin susceptible and colistin resistant	among the combinations of 0.5× MIC antimicrobial agents, colistin plus tigecycline showed synergistic or bactericidal effects against four *A. baumannii* isolates
Sheng *et al.* (2011)[60]	tigecycline	*in vitro*	carbapenem-resistant AB, colistin susceptible	the combination of tigecycline and colistin showed good *in vitro* synergy against carbapenem-resistant AB with high imipenem resistance
Santimaleewogragun *et al.* (2011)[63]	fosfomycin or imipenem or sulbactam	*in vitro*	carbapenem-resistant AB, colistin susceptible	a chequerboard assay showed the synergistic effects of colistin plus fosfomycin against 12.5% of eight isolates; no synergism between colistin and sulbactam, colistin and imipenem against the tested isolates
Hornsey *et al.* (2011)[69]	glycopeptide (vancomycin and teicoplanin)	*in vivo*	MDR AB, colistin susceptible	glycopeptide/colistin combinations are highly active both *in vitro* and in a simple animal (*G. mellonella*) model of infection
Shields *et al.* (2010)[70]	carbapenem	*in vitro*/case report	XDR AB, colistin susceptible	carbapenem/colistin combination proved to be effective against strains isolated from transplant patients; when this combination was given to these patients, 80% (4/5) of them were treated successfully
Ozbek *et al.* (2010)[71]	tigecycline	*in vitro*	meropenem-resistant AB	a synergistic interaction was observed for tigecycline/colistin; tigecycline slightly changed the post-antibiotic effect of colistin
Candel *et al.* (2010)[72]	tigecycline + meropenem	case report	MDR AB, colistin susceptible	a renal transplant recipient who developed bacteraemia had a favourable clinical outcome with a tigecycline/colistin/meropenem combination
Rodriguez *et al.* (2010)[14]	rifampicin or imipenem	*in vitro*	carbapenem-resistant AB, colistin heteroresistant	colistin/rifampicin and colistin/imipenem were synergistic against heteroresistant isolates and prevented the development of colistin-resistant mutants
Pongpech *et al.* (2010)[73]	imipenem or imipenem + sulbactam	*in vitro*	MDR AB, colistin susceptible	imipenem/colistin showed best synergy effects, while addition of sulbactam to meropenem and colistin may further improve their antibacterial activity
Pachon-Ibanez *et al.* (2010)[74]	rifampicin	*in vitro*/*in vivo*	MDR AB, colistin susceptible	rifampicin/colistin showed efficacy *in vitro* and in experimental models of pneumonia and meningitis

Yun Cai et al. JAC , 2012 Colistin resistance of *Acinetobacter baumannii*: clinical reports, mechanisms and antimicrobial strategies

Rifampin açık ara önde...

Dizbay *et al.* (2010)[75]	tigecycline	*in vitro*	XDR AB, colistin susceptible	the tigecycline/colistin combination was more synergistic than tigecycline/rifampicin and colistin/rifampicin according to the FIC index
Principe *et al.* (2009)[58]	tigecycline	*in vitro*	tigecycline-non-susceptible AB	tigecycline/colistin was synergistic against five of seven strains
Arroyo *et al.* (2009)[29]	tigecycline	*in vitro*	colistin-susceptible and colistin-resistant AB	FIC of tigecycline/colistin for 35 *A. baumannii* isolates (selected by colistin MICs of 0.12 to 4 mg/L) ranged from 0.75 to 2
Lee *et al.* (2008)[76]	meropenem or sulbactam or meropenem + sulbactam	*in vitro*/case report	MDR AB, colistin susceptible	combined colistin with meropenem and/or sulbactam can inhibit bacterial regrowth at 24 h
Song *et al.* (2008)[77]	rifampicin	case report	carbapenem-resistant AB, colistin susceptible	7 (70%) of 10 patients with ventilator-associated pneumonia benefitted from colistin/rifampicin therapy; six patients were cured microbiologically
Bassetti *et al.* (2008)[78]	rifampicin	case report	MDR AB, colistin susceptible	clinical and microbiological responses were observed in 22 of 29 (76%) critically ill patients with pneumonia and bacteraemia treated with colistin/rifampicin
Pankuch *et al.* (2008)[57]	meropenem	*in vitro*	colistin-susceptible and colistin-resistant AB	subinhibitory meropenem/colistin showed synergy against 49 of 52 strains at 24 h
Pantopoulou *et al.* (2007)[79]	rifampicin	*in vivo*	MDR AB, colistin susceptible	colistin's activity in prolonging survival in an experimental thigh infection in neutropenic rats was enhanced after co-administration with rifampicin
Biancofiore *et al.* (2007)[80]	meropenem + rifampicin	case report	MDR AB, colistin susceptible	colistin/rifampicin/meropenem successfully treated a case of multifocal (lungs, skin, soft tissues) infection
Timurkaynak *et al.* (2006)[61]	rifampicin or meropenem or azithromycin or doxycycline	*in vitro*	MDR AB, colistin susceptible	colistin/rifampicin was fully synergistic against four of five isolates; colistin/meropenem and colistin/azithromycin each showed synergistic activity against three of five isolates; colistin/doxycycline was partially synergistic or additive against five isolates
Motaouakkil *et al.* (2006)[81]	rifampicin	clinical trial	MDR AB, colistin susceptible	colistin/rifampicin was favourable for all 26 nosocomial infection patients
Petrosillo *et al.* (2005)[82]	rifampicin or rifampicin + ampicillin/sulbactam	case report	carbapenem-resistant AB, colistin susceptible	therapy with colistin/rifampicin, and with ampicillin/sulbactam in case of susceptibility to this combination, resulted in microbiological clearance of carbapenem-resistant AB in 9 (64%) of 14 critically ill patients, with limited side effects
Fulnecky *et al.* (2005)[62]	amikacin	case report	MDR AB, colistin susceptible	a 52-year-old man with post-surgical meningitis experienced successful clinical and microbiological outcomes following colistin/amikacin therapy
Montero *et al.* (2004)[83]	rifampicin	*in vitro*	carbapenem-resistant AB, colistin susceptible	for strains highly resistant to imipenem and moderately resistant to rifampicin, colistin/rifampicin may be useful
Hogg *et al.* [84]	rifampicin	*in vitro*	MDR AB, colistin	colistin/rifampicin was synergistic against 11 of 13 isolates

Yun Cai et al. JAC , 2012 Colistin resistance of *Acinetobacter baumannii*: clinical reports, mechanisms and antimicrobial strategies

Rifampin ≥19 mm → Duyarlı

Tableau IX – Concentrations, diamètres critiques et règles de lecture interprétative pour *Acinetobacter* spp., *Stenotrophomonas maltophilia* et *Burkholderia cepacia*.

Antibiotique	Charge du disque	Concentrations critiques (mg/L) S	R	Diamètres critiques (mm) S	R	Remarques
Sulbactam		≤ 8	-			Activité antibactérienne propre à évaluer par détermination de la CMI pour *Acinetobacter* spp. et *B. cepacia*.
Ticarcilline	75 µg	≤ 16	> 64	≥ 22	< 18	Pour *Acinetobacter* spp.
Ticarcilline/ac. clavulanique	75/10 µg	≤ 16/2	> 64/2	≥ 22	< 18	Pour *Acinetobacter* spp. et *S. maltophilia*.
Pipéracilline	75 µg	≤ 16	> 64	≥ 18	< 12	Pour *Acinetobacter* spp. et *B. cepacia*.
Pipéracilline/tazobactam	75/10 µg	≤ 16/4	> 64/4	≥ 19	< 14	Pour *Acinetobacter* spp.
Imipénème	10 µg	**≤ 2**	**> 8**	***≥ 24***	***< 17***	
Méropénème	10 µg	**≤ 2**	**> 8**	***≥ 22***	***< 15***	
Doripénème	**10 µg**	***≤ 1***	***> 4***	***≥ 24***	***< 19***	
Ceftazidime	30 µg	**≤ 4**	**> 8**	***≥ 21***	***< 19***	Synergie possible sulbactam + ceftazidime pour *Acinetobacter* spp.
Céfépime	30 µg	**≤ 4**	**> 8**	***≥ 21***	***< 19***	Synergie possible sulbactam + céfépime pour *Acinetobacter* spp.
Cefpirome	30 µg	**≤ 4**	**> 8**	***≥ 21***	***< 19***	Synergie possible sulbactam + cefpirome pour *Acinetobacter* spp.
Tobramycine	10 µg	**≤ 4**	**> 4**	**≥ 16**	**< 16**	Pour *Acinetobacter* spp.
Amikacine	30 µg	**≤ 8**	**> 16**	**≥ 17**	**< 15**	Pour *Acinetobacter* spp.
Isépamicine	30 µg	≤ 8	> 16	≥ 17	< 15	Pour *Acinetobacter* spp.
Gentamicine	15 µg (10 UI)	**≤ 4**	**> 4**	**≥ 16**	**< 16**	Pour *Acinetobacter* spp.
Nétilmicine	30 µg	**≤ 4**	**> 4**	**≥ 19**	**< 19**	Pour *Acinetobacter* spp.
Chloramphénicol	30 µg	≤ 8	> 16	≥ 23	< 19	Interprétation valable pour thiamphénicol.
Tétracycline	30 UI	≤ 4	> 8	≥ 19	< 17	Pour *S. maltophilia* et *B. cepacia*.
Colistine	50 µg	**≤ 2**	**> 2**	**≥ 15**	**< 15**	Les diamètres ont pour but de vérifier la résistance naturelle de certaines espèces, mais ne permettent pas de détecter toutes les résistances acquises ce qui impose de déterminer la CMI en cas d'utilisation thérapeutique (souche multirésistante). Interprétation valable pour polymyxine B.
Péfloxacine	5 µg	≤ 1	> 4	≥ 22	< 16	
Ofloxacine	5 µg	≤ 1	> 1	≥ 22	< 22	La résistance aux fluoroquinolones est croisée entre les différentes molécules mais son niveau d'expression peut varier pour chaque molécule.
Ciprofloxacine	5 µg	**≤ 1**	**> 1**	**≥ 22**	**< 22**	
Lévofloxacine	5 µg	**≤ 1**	**> 2**	**≥ 20**	**< 17**	
Rifampicine	30 µg	≤ 4	> 16	≥ 19	< 14	Pour *Acinetobacter* spp. et *S. maltophilia*.
Triméthoprime/sulfaméthoxazole	1,25/23,75 µg					Interprétation valable uniquement pour les autres associations triméthoprime-sulfamide.
- *S. maltophilia*		**≤ 4/76**	**> 4/76**	***≥ 13***	***< 13***	
- Autres espèces		**≤ 2/38**	**> 4/76**	***≥ 16***	***< 13***	

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Kolistin + Vankomisin, Kolistin + Kotrimoksazol → KDAB için bakterisidal

Antimicrob Agents Chemother. 2012 Sep;56(9):4856-61. doi: 10.1128/AAC.05996-11. Epub 2012 Jul 2.

In vitro synergy of colistin combinations against colistin-resistant Acinetobacter baumannii, Pseudomonas aeruginosa, and Klebsiella pneumoniae isolates.

Vidaillac C[1], Benichou L, Duval RE.

Author information

Abstract

Colistin resistance, although uncommon, is increasingly being reported among Gram-negative clinical pathogens, and an understanding of its impact on the activity of antimicrobials is now evolving. We evaluated the potential for synergy of colistin plus trimethoprim, trimethoprim-sulfamethoxazole (1/19 ratio), or vancomycin against 12 isolates of Acinetobacter baumannii (n = 4), Pseudomonas aeruginosa (n = 4), and Klebsiella pneumoniae (n = 4). The strains included six multidrug-resistant clinical isolates, K. pneumoniae ATCC 700603, A. baumannii ATCC 19606, P. aeruginosa ATCC 27853, and their colistin-resistant derivatives (KPm1, ABm1, and PAm1, respectively). Antimicrobial susceptibilities were assessed by broth microdilution and population analysis profiles. The potential for synergy of colistin combinations was evaluated using a checkerboard assay, as well as static time-kill experiments at 0.5× and 0.25× MIC. The MIC ranges of vancomycin, trimethoprim, and trimethoprim-sulfamethoxazole (1/19) were ≥128, 4 to ≥128, and 2/38 to >128/2,432 μg/ml, respectively. Colistin resistance demonstrated little impact on vancomycin, trimethoprim, or trimethoprim-sulfamethoxazole MIC values. Isolates with subpopulations heterogeneously resistant to colistin were observed to various degrees in all tested isolates. In time-kill assays, all tested combinations were synergistic against KPm1 at 0.25× MIC and 0.5× MIC and ABm1 and PAm1 at 0.5× MIC. In contrast, none of the tested combinations demonstrated synergy against any colistin-susceptible P. aeruginosa isolates and clinical strains of K. pneumoniae isolates. Only colistin plus trimethoprim or trimethoprim-sulfamethoxazole was synergistic and bactericidal at 0.5× MIC against K. pneumoniae ATCC 700603. Colistin resistance seems to promote the in vitro activity of unconventional colistin combinations. Additional experiments are warranted to understand the clinical significance of these observations.

Uyarı: Klinik uygulamadaki dozlar ile Kotrimoksazol, vankomisin sinerjisi kesin değil

TABLE 1 Antimicrobial susceptibility

Isolate	MIC (μg/ml)[a]			
	CST	VAN	TMP	TMP/SMX (1/19)
A. baumannii				
ATCC 19606	1	>128	32	16/304
ABm1	8	128	32	16/306
AB1	0.5	>128	64	8/152
AB2	1	>128	>128	>128/2,432
K. pneumoniae				
ATCC 700603	0.5	>128	4	2/38
KPm1	32	>128	4	2/38
KP3	0.5	>128	>128	>128/2,432
KP4	0.5	>128	>128	>128/2,432
P. aeruginosa				
ATCC 27853	0.5	>128	>128	>128/2,432
PAm1	8	>128	>128	32/612
PA4	0.5	128	>128	>128/2,432
PA5	1	128	>128	>128/2,432

[a] CST, colistin; VAN, vancomycin; TMP, trimethoprim; SMX, sulfamethoxazole.

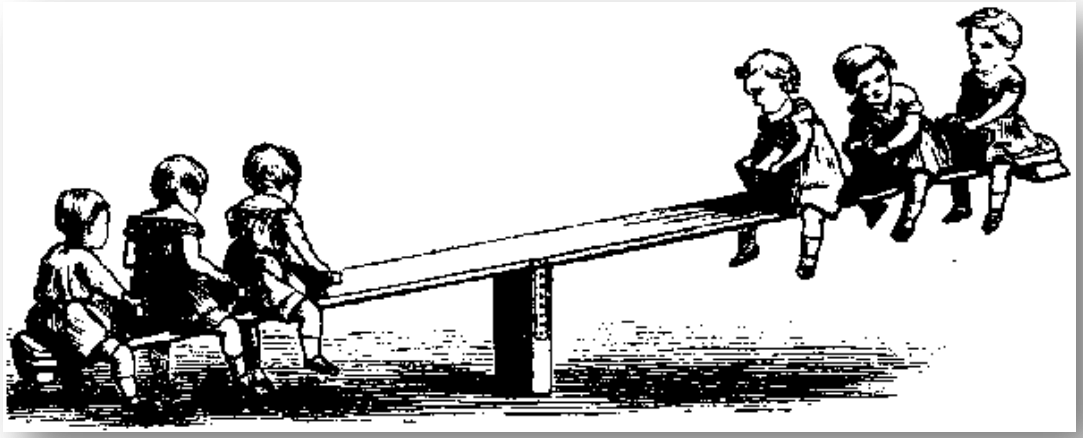


TABLE 2 *In vitro* evaluation of the bacteriostatic (checkerboard assay) and bactericidal activity (time-kill assay) of colistin combinations at 0.5× and 0.25× MIC[a]

Isolate	CST + VAN			CST + TMP			CST + TMP/SMX (1/19)		
	0.5× MIC	0.25× MIC	ΣFIC	0.5× MIC	0.25× MIC	ΣFIC	0.5× MIC	0.25× MIC	ΣFIC
A. baumannii									
ATCC 19606	−4.72 ± 0.05	−4.70 ± 0.03	0.25	−4.33 ± 0.33	+3.46 ± 0.36	0.50	−4.40 ± 0.27	+3.65 ± 0.60	0.37
ABm1	−4.74 ± 0.01	−4.61 ± 0.13	0.18	−4.83 ± 0.01	−0.71 ± 0.37	0.37	−4.23 ± 0.07	+2.15 ± 0.38	0.20
AB1	−4.54 ± 0.10	−1.26 ± 0.63	0.50	−4.25 ± 0.78	+3.03 ± 0.36	0.5	−4.65 ± 0.12	+3.05 ± 0.40	0.37
AB2	−4.88 ± 0.13	−4.74 ± 0.18	0.37	−2.66 ± 0.36	+3.42 ± 0.17	0.37	−2.04 ± 0.36	+3.21 ± 0.41	0.5

Kolistin direncine yol açan değişimler sıradışı antibiyotik sinerjilerini bozmuyor

Antimicrob Agents Chemother. 2015 Aug;59(8):4544-50. doi: 10.1128/AAC.00753-15. Epub 2015 May 18.

Colistin and Fusidic Acid, a Novel Potent Synergistic Combination for Treatment of Multidrug-Resistant Acinetobacter baumannii Infections.

Phee LM[1], Betts JW[2], Bharathan B[3], Wareham DW[1].

⊕ Author information

Abstract

The spread of multidrug-resistant Acinetobacter baumannii (MDRAB) has led to the renaissance of colistin (COL), often the only agent to which MDRAB remains susceptible. Effective therapy with COL is beset with problems due to unpredictable pharmacokinetics, toxicity, and the rapid selection of resistance. Here, we describe a potent synergistic interaction when COL was combined with fusidic acid (FD) against A. baumannii. Synergy in vitro was assessed against 11 MDRAB isolates using disc diffusion, checkerboard methodology (fractional inhibitory concentration index [FICI] of ≤ 0.5, susceptibility breakpoint index [SBPI] of >2), and time-kill methodology (≥2 log10 CFU/ml reduction). The ability of FD to limit the emergence of COL resistance was assessed in the presence and absence of each drug alone and in combination. Synergy was demonstrated against all strains, with an average FICI and SBPI of 0.064 and 78.85, respectively. In time-kill assays, COL-FD was synergistic and rapidly bactericidal, including against COL-resistant strains. Fusidic acid prevented the emergence of COL resistance, which was readily selected with COL alone. This is the first description of a novel COL-FD regimen for the treatment of MDRAB. The combination was effective at low concentrations, which should be therapeutically achievable while limiting toxicity. Further studies are warranted to determine the mechanism underlying the interaction and the suitability of COL-FD as an unorthodox therapy for the treatment of multidrug-resistant Gram-negative infections.

Kolistin/Fusidik asit

Kolistin dirençli tüm kökenlerde sinerjik
Hızlı bakterisidal
Ortalama FİKİ 0.064 (<0.5)
Ortalama Duraylılık Sınır değer İndeksi 78.85 (>2)
Kolistin duyarlı kökenlerde kolistin monoterapisi ile seçilen **kolistin direncinin gelişmesini ÖNLÜYOR**
Klinik rutin dozlar yeterli

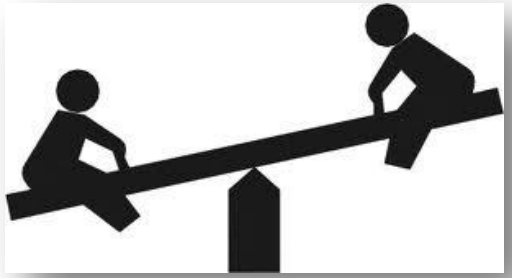
Combination Therapy is recommended for all patients prescribed colistin. Our current preference is either imipenem-cilastatin or meropenem. If the patient is allergic to carbapenems, then combine with rifampin. No clinical data to support triple therapy

- Imipenem-cilastatin or meropenem may show increased activity, even in the presence of carbapenemases OR
- Rifampin 600 mg IV/po once daily reported most often
  - Due to the detergent effect of colistin on the cell wall, the activity of many antibiotics is enhanced (BMC Inf Dis 11:109, 2011; Int J Antimicrob Agents 37:244, 2011)
  - Combinations reported as synergistic, additive, and even antagonistic
  - Combinations may help prevent, or slow, selection of colistin-resistant subpopulations

- In vitro exposure to polymyxin B or E (colistin) results in rapid selection of resistant subpopulations; same phenomena noted in infected animal models. Refs: AAC 54:3783, 2010 and JAC 65:1984, 2010.
- Slower selection of resistance with more frequent dosing.
- In vitro, minocycline prevented the emergence of resistance and augmented colistin antibacterial activity; tigecycline may function similarly but no data.
- Synergy with rifampin vs *P. aeruginosa* or *Acinetobacter baumannii* is unpredictable.
- Antibacterial activity is concentration-dependent BUT there is little or no post-antibiotic effect. Further, nephrotoxicity is concentration and time dependent. Animal model data is inconsistent. Hence, at lease at the present time once daily dosing is NOT recommended.
- Interesting "seesaw" effect of colistin vs *A. baumannii*. The greater the resistance to colistin the greater the susceptibility to beta-lactams and glycopeptides. Refs: CID 45:594, 2007; CID 46:1324, 2008; JAC 66:1047, 2011.

SEESAW=TAHTEREVALLİ ETKİSİ

Kolistin-dirençli A.baumannii kökenlerinde diğer antibiyotiklerin MİK'leri belirgin düşüyor



Antibiotic	Tested concentration range, μg/mL	Breakpoint for susceptible strains, μg/mL	MIC, μg/mL (no. of strains with MIC)	
			Parent strains	Colistin-resistant strains
Penicillins				
Ampicillin	2–32	≤8	16 (2), ≥32 (15)	2 (3), 4 (8), 16 (3), ≥32 (3)
Amoxicillin–clavulanic acid	2/1–32/16	NB	4 (3), 16 (2), ≥32 (12)	≤2 (13), 4 (2), 8 (1), ≥32 (1)
Ticarcillin–clavulanic acid	8/2–128/2	≤16	≤8 (4), 16 (1), ≥128 (12)	≤8 (16), ≥32 (1)
Piperacillin-tazobactam	4/4–128/4	≤16	≤4 (5), 64 (12)	≤4 (16), 64 (1)
Benzylpenicillin	0.03–0.5	NB	≥0.5 (17)	≥0.5 (17)
Oxacillin	0.25–4	NB	≥4 (17)	≥4 (17)
Cephalosporins				
Cefalotin	2–64	NB	≥64 (17)	≤2 (2), 8 (1), ≥64 (14)
Cefazolin	4–64	NB	≥64 (17)	≤4 (3), 16 (4), 32 (2), ≥64 (8)
Cefoxitin	4–64	NB	≥64 (17)	≤4 (9), 8 (2), 16 (1), 32 (2), ≥64 (3)
Ceftazidime	1–64	≤8	4 (1), 8 (3), 16 (1), ≥64 (12)	≤1 (12), 2 (1), 4 (2), 16 (1), ≥64 (1)
Ceftriaxone	1–64	≤8	8 (1), 16 (3), 32 (1), ≥64 (12)	≤1 (10), 2 (1), 4 (2), 8 (2), 16 (1), ≥64 (1)
Cefepime	1–64	≤8	2 (1), 4 (2), 8 (2), 16 (11), 32 (1)	≤1 (15), 2 (1), 16 (1)
Carbapenems				
Meropenem	0.25–16	≤4	≤0.25 (4), 0.5 (1), 8 (11), ≥16 (1)	≤0.25 (16), 4 (1)
Imipenem	1–16	≤4	≤1 (5), 8 (11), ≥16 (1)	≤1 (17)
Aminoglycosides				
Amikacin	2–64	≤16	≤2 (13), 4 (1), 8 (2), 16 (1)	≤2 (17)
Gentamicin	1–16	≤4	≤1 (3), 2 (1), 8 (1), ≥16 (12)	≤1 (5), 2 (1), 4 (5), 8 (1), ≥16 (5)
Tobramycin	1–16	≤4	≤1 (14), 2 (1), 4 (1), 8 (1)	≤1 (17)
Quinolones				
Nalidixic acid	2–32	NB	4 (5), ≥32 (12)	≤2 (3), 4 (2), 8 (2), 16 (8), ≥32 (2)
Ciprofloxacin	0.25–4	≤4	≤0.25 (2), 0.5 (2), 2 (1), ≥4 (12)	≤0.25 (4), 0.5 (2), 1 (8), 2 (1), ≥4 (2)
Norfloxacin	0.5–16	≤4	2 (4), 8 (1), ≥16 (12)	≤0.5 (2), 1 (2), 2 (8), 4 (3), ≥16 (2)
Sulphonamides and trimethoprim				
Trimethoprim	0.5–16	≤2	8 (2), ≥16 (15)	8 (1), ≥16 (16)
Trimethoprim-sulfamethoxazole	20 (1/19)–320 (16/304)	≤2/38	≤20 (4), ≥320 (13)	≤20 (4), 80 (1), 160 (1), ≥320 (11)
Macrolides and lincosamides				
Erythromycin	0.25–8	NB	≥8 (17)	≤0.25 (12), 0.5 (4), ≥8 (1)
Clindamycin	0.25–8	NB	≥8 (17)	0.5 (1), 4 (4), ≥8 (12)
Streptogramins: quinupristin-dalfopristin	0.25–16	NB	≥16 (17)	0.5 (1), 1 (8), 2(7), 8 (1)
Glycopeptides				
Teicoplanin	0.5–32	NB	≥32 (17)	≤0.5 (14), 1 (1), 2 (2)
Vancomycin	1–32	NB	≥32 (17)	≤1 (6), 8 (4), 16 (1), ≥32 (6)
Tetracycline	1–16	NB	4 (2), 8 (1), ≥16 (14)	≤1 (2), 2 (1), ≥16 (14)
Rifamycins: rifampicin	0.5–32	NB	2 (1), 16 (2), ≥32 (14)	≤0.5 (12), 1 (5)
Oxazolidinones: linezolid	0.5–8	NB	≥8 (17)	≥8 (17)
Other				
Fusidic acid	0.5–32	NB	≥32 (17)	≤0.5 (8), 1 (6), 2 (2), ≥32 (1)
Nitrofurantoin	16–512	NB	256 (1), ≥512 (16)	32 (1), 64 (1), 128 (1), 256 (6), ≥512 (8)

NOTE. NB, no breakpoint data were available for these antibiotics against *Acinetobacter baumannii*.

Jian Li et al. Clin Infect Dis. 2007;45:594-598

Clinical Infectious Diseases

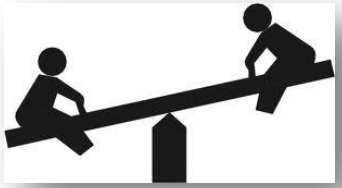
MIC50, antimicrobial susceptibility profile, and susceptibility rates of 3683 polymyxin-susceptible and 24 polymyxin-resistant Acinetobacter baumannii isolates.

Antimicrobial agent	Polymyxin-susceptible phenotype[a]		Polymyxin-resistant phenotype[a]		P[b]	OR (95 CI%)[c]
	MIC_{50}, μg/mL	Susceptibility rate, %	MIC_{50}, μg/mL	Susceptibility rate, %		
Ampicillin-sulbactam	16	45.4	4	70.8	.013	2.92 (1.14–7.76)
Piperacillin	>64	21.0	64	33.3	.138	1.88 (0.74–4.69)
Piperacillin-tazobactam	>64	33.2	32	45.8	.187	1.71 (0.71–4.07)
Ticarcillin-clavulanate	128	29.3	64	33.3	.762	1.14 (0.54–2.83)
Aztreonam	>16	4.9	>16	20.8	<.001	5.21 (1.68–15.0)
Cefoxitin	>16	0.9	>16	20.8	<.001	30.0 (9.18–92.4)
Cefepime	16	38.4	4	58.3	.046	2.24 (0.93–5.44)
Ceftazidime	>16	34.5	>16	45.8	.240	1.61 (0.67–3.84)
Ceftriaxone	>32	16.2	32	41.6	<.001	3.7 (1.52–8.89)
Cefuroxime	>16	2.6	>16	25.0	<.001	12.72 (4.41–34.97)
Imipenem	1	71.6	1	66.6	.589	0.79 (0.32–2.02)
Meropenem	2	68.0	4	58.3	.314	0.66 (0.28–1.60)
Ciprofloxacin	>4	32.7	1	50.0	.072	2.06 (0.86–4.90)
Levofloxacin	>4	35.6	≤0.5	50.0	.142	1.81 (0.76–4.31)
Amikacin	32	48.8	8	58.3	.355	1.46 (0.61–3.55)
Gentamicin	>8	37.0	4	50.0	.190	1.70 (0.71–4.05)
Tobramycin	4	53.8	8	45.8	.434	0.73 (0.30–1.73)
Minocycline	≤1	88.4	≤1	87.5	.885	0.91 (0.26–3.89)
Tigecycline	0.5	97.0	0.5	95.8	.729	0.70 (0.10–14.16)
Doxycycline	≤1	74.6	≤1	87.5	.150	2.37 (0.67–10.03)
Tetracycline	8	43.1	≤4	58.3	.133	1.85 (0.77–4.49)
Trimethoprim-sulfamethoxazole	>2	37.9	≤2	54.2	.420	1.39 (0.58–3.31)

[a] The category of susceptibility for polymyxin was determined as specified by the Clinical and Laboratory Standards Institute [5], except for tigecycline, which was interpreted according to the breakpoints approved by the US Food and Drug Administration (≤2 μg/mL for susceptible and ≥8 μg/mL for resistant).

[b] Calculated by χ^2 test.

[c] ORs and respective 95% CIs refer to comparisons of susceptibility rates between polymyxin-resistant *A. baumannii* and polymyxin-susceptible *A. baumannii* for each antimicrobial agent.



Rodrigo E. Mendes et al. Clin Infect Dis. 2008;46:1324-1326

Yeni tedavi hedefleri

YENİ PEPTİDLER

Cecropin A–melittin hybrid

→ KDAB kökenlerinde LPS'ye afinitesi kolistinden fazla

→ Hızlı bakterisidal

Rodríguez-Hernández *et al.* JAC 2006

Mastoparan → Kolistin duyarlı ve dirençli A. baumannii kökenlerinde MİK'in 8 katına çıkarak **BAKTERİSİDAL** etki gösterir

Bu yeni peptidlerin etki mekanizması tam bilinmiyor

Vila-Farres*et al.* Eur J Med Chem. 2015

Monoklonal antikor tedavisi

Abstract ▾ Send to: ▾

Indian J Med Res. 2010 Apr;131:578-83.

Iron regulated outer membrane proteins (IROMPs) as potential targets against carbapenem-resistant Acinetobacter spp. isolated from a Medical Centre in Malaysia.

Hwa WE[1], Subramaniam G, Mansor MB, Yan OS, Gracie, Anbazhagan D, Devi SS.

⊕ Author information

Abstract

BACKGROUND & OBJECTIVES: Carbapenem-resistant Acinetobacter spp. have gained increasing significance as opportunistic pathogens in hospitalized patients. Carbapenem resistance is often associated with the loss and/or decrease in outer membrane proteins (OMP) and overexpression of multidrug efflux systems. However, carbapenem-hydrolysing beta-lactamases of Ambler Class B (metallo-enzymes) and Ambler Class D (oxacillinases) have also been detected in Acinetobacter spp. In this study we have investigated the role of the iron regulated outer membrane protein (IROMPs) and the loss of a 29-kDa OMP in carbapenem resistance of Acinetobacter calcoaceticus.

METHODS: Carbapenem resistant clinical isolates (n=39) of Acinetobacter baumannii / calcoaceticus were used. Identification of Acinetobacter spp. at species level was done by amplified ribosomal DNA restriction analysis (ARDRA). MIC was evaluated using agar dilution method according to CLSI standards. Presence of outer membrane proteins were determined by SDS-PAGE. A representative strain of A. calcoaceticus, S26 with the loss of 29-kDa OMP was selected for further analysis as strain S26 had unique resistance mechanism, that is, the presence of IMP-4 metallo-beta-lactamases. IROMPs were expressed under iron deficit conditions. Bands corresponding to IROMPs were excised from SDS-PAGE and used to immunize rabbits for the production of polyclonal antibodies. The antibodies raised against IROMPs were detected by an in-house ELISA and then used for bactericidal activity against carbapenem resistant A. baumannii / calcoaceticus.

RESULTS: All isolates were resistant to all antibiotics including imipenem and meropenem and had loss of a 29-kDa OMP. The polyclonal antibodies showed bactericidal effect against the organism tested and it specifically killed the bacteria grown in iron deficit medium.

INTERPRETATION & CONCLUSIONS: In this study, a 29-kDa OMP has been identified to be the major outer membrane protein in A. baumannii / calcoaceticus and loss of this porin and overexpression of IROMPs have contributed to carbapenem resistance. Polyclonal antibodies raised against IROMPs may have a role in antimicrobial therapy in these isolates.

Patojen bakteriler, çoğalıp enfeksiyon oluşturmak için demire ihtiyaç duyar. Demiri elde edebilmek için konağın demir bağlayan proteinleri (heme, ferritin, transferrin, hemosiderin)ile yarışmak zorundadır.

Bakteri "siderofor" adı verilen düşük molekül ağırlıklı yüksek afiniteli demir şelatörleri ve bunların özgül yüzey reseptörlerini Iron Regulated Outer Membrane Proteins (IROMPs) salgılar.

Bu reseptörler demirin kısıtlı oluğu durumlarda eksprese olur. Acinetobacter dışında *Escherichia coli*, *Pseudomonas aeruginosa* ve *Neisseria gonorrheae*'de de IROMPların rolü gösterilmiştir.

İşte bu proteinlere karşı geliştirilen monoklonal antikorlar, siderofor aracılı demir alımını bloke ederek bakteriyostatik hatta bakterisidal etki oluşturur.

BMC Microbiol. 2001;1:16. Epub 2001 Aug 9.

Monoclonal antibodies against the iron regulated outer membrane Proteins of Acinetobacter baumannii are bactericidal.

Goel VK[1], Kapil A.

Author information

Abstract

BACKGROUND: Iron is an important nutrient required by all forms of life.In the case of human hosts,the free iron availability is 10(-18) M,which is far less than what is needed for the survival of the invading bacterial pathogen. To survive in such conditions, bacteria express new proteins in their outer membrane and also secrete iron chelators called siderophores. RESULTS/ DISCUSSION: Acinetobacter baumannii ATCC 19606, a nosocomial pathogen which grows under iron restricted conditions, expresses four new outer membrane proteins,with molecular weight ranging from 77 kDa to 88 kDa, that are called Iron Regulated Outer Membrane Proteins (IROMPs). We studied the functional and immunological properties of IROMPs expressed by A.baumanii ATCC 19606. The bands corresponding to IROMPs were eluted from SDS-PAGE and were used to immunize BALB/c mice for the production of monoclonal antibodies. Hybridomas secreting specific antibodies against these IROMPs were selected after screening by ELISA and their reactivity was confirmed by Western Blot. The antibodies then generated belonged to IgM isotype and showed bactericidical and opsonising activities against A.baumanii in vitro. These antibodies also blocked siderophore mediated iron uptake via IROMPs in bacteria.

CONCLUSION: This proves that iron uptake via IROMPs,which is mediated through siderophores,may have an important role in the survival of A.baumanii inside the host,and helps establishing the infection.

PMID: 11532195 [PubMed - indexed for MEDLINE] PMCID: PMC48144 Free PMC Article

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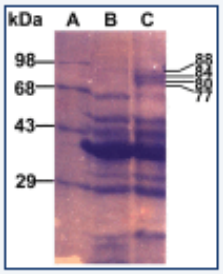

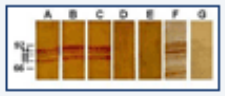

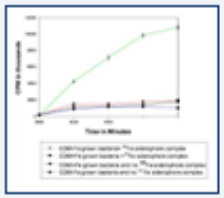

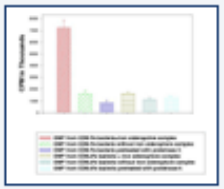

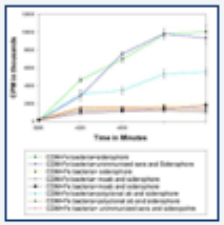

DİKKAT...DİKKAT...DİKKAT...

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Hot Topic

Emergence of colistin-resistant bacteria in humans without colistin usage: a new worry and cause for vigilance

Abiola Olumuyiwa Olaitan
Serge Morand[a, b]
Jean-Marc Rolain

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doi:10.1016/j.ijantimicag.2015.11.009

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Kolistin maruziyeti olmayan hastalarda kolistin direnci

1) **Kolistin ile** insan katyonik antimikrobiyalleri (**lizozim**, LL-37) arasındaki çapraz direnç

konağın doğal immünitesinin bakterilere maruziyeti

→ lizozim aktivitesi

2) Kolistin dirençli bakterilerin hayvansal gıdalar yoluyla alınması

Kolistin veterinerlikte sıkça kullanılmaktadır

(Domuz çifliklerinde E.coli ishallerini ve septisemisini önlemek için)

3) Plazmid aracılı kolistin direnci aktarımı → E.coli, Klebsiella→ Çin

TEŞEKKÜR EDERİM