In Vitro Activities of Nine Current Antibiotics against Culprit Bacteria in Nosocomial Infections in an Institution in Northern Taiwan

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Background: In recent years, there has been a rapid worldwide emergence of multidrug-resistant (MDR) pathogens, especially in cases of nosocomial infections. This study assesses the in vitro activities of ampicillin/sulbactam, cefpirome, colistin, daptomycin, ertapenem, meropenem, teicoplanin, tigecycline and vancomycin against 208 aerobic bacterial pathogens that caused 197 nosocomial infections in 184 patients.

Methods: Antimicrobial susceptibility was evaluated by Etest. Broth dilution method was utilized in tigecycline susceptibility testing.

Results: Most (140/208, 67%) of the isolates were facultative Gram-negative bacilli. Of the 31 oxacillin-resistant *S. aureus* (ORSA) isolates, 16 were susceptible to daptomycin (16/31, 51.6%) according to the breakpoint ≦ 1 μg/ml. All 31 ORSA isolates were susceptible to teicoplanin, and vancomycin but MICs of vancomycin for all 31 ORSA isolates were ≧ 1 μg/ml. Of the 21 isolates of *A. baumannii* that were multiple-drug-resistant, 19 isolates (19/21, 90%) were susceptible to colistin and 18 isolates (18/21, 86%) sensitive to tigecycline. Of the 22 isolates of *E. coli* with extended-spectrum beta-lactamase (ESBL), the most susceptible antimicrobial agent were colistin (20/22, 91%), ertapenem (21/22, 96%), meropenem and tigecycline (22/22, 100%). Of the 11 isolates of *P. aeruginosa,* 6 isolates were susceptible to colistin (6/11, 55%) and all isolates were susceptible to meropenem (11/11, 100%).

Conclusion: For nosocomial infections caused by MDR-*Acinetobacter baumannii,* colistin and tigecycline are usually susceptible according to the result of this study. For nosocomial infections caused by ORSA, ORSA has reduced susceptibility to vancomycin, teicoplanin and daptomycin. For MDR-*P. aeruginosa,* further study is needed.

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Key words: in-vitro activities, nine current antibiotics, nosocomial isolates

The emergence of antimicrobial resistance to cephalosporins and quinolone among Gram-negative bacteria has complicated the treatment of many serious infections. In recent years there has been a

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rapid worldwide emergence of multidrug-resistant (MDR)-pathogens. Pathogens of concern to clinicians include extended-spectrum β-lactamase (ESBL) and quinolone-resistant *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Serratia marcescens,* and *Citrobacter freundii,* oxacillin-resistant *Staphylococcus aureus* (ORSA), MDR-*Pseudomonas aeruginosa* and MDR-*Acinetobacter baumannii*.[1-8] With continued antibiotic selective pressure in clinical settings, particularly in hospitals, pathogens resistant to these agents have posed considerable problems.[9,10]

Antimicrobial resistance is a global problem[5,11] and Taiwan is no exception.[11,12] In Taiwan, MDR-*A. baumannii,* MDR-*P. aeruginosa* and MDR-Enterobactericeae with ESBL have emerged, especially in nosocomial infections.[12] A 1999 report by the National Nosocomial Infections Surveillance system disclosed a remarkable increase in the prevalence of most of these resistant pathogens in ICU patients compared with the previous 5 years.[12] A similar epidemiological trend has been documented in several medical centers in Taiwan. From September through November, 2005, a nationwide surveillance of clinically significant bacteria from the ICUs of major teaching hospitals in Taiwan investigated the susceptibilities of these bacteria to carbapenems and revealed an increase in MDR-bacteria, particularly Enterobacteriaceae.[13] However, the incidence of antimicrobial resistance among these clinically significant pathogens varies considerably among countries, among hospitals within one country, and even among different wards within one hospital. We have already studied and reported the in vitro activities of levofloxacin, ciprofloxacin, ceftazidime, cefepime, imipenem and piperacillin-tazobactam against aerobic bacterial pathogens isolated from patients with nosocomial infections.[14] However MDR-bacteria, especially MDR-*Acinetobacter baumannuii* and -*Pseudomonas aeruginosa,* have emerged in our hospitals and other hospitals in Taiwan.[12] Thus, we conducted this study to focus primarily on isolates of nosocomial Infections. The objectives of this study were to assess and compare the in vitro activities of ampicillin/sulbactam, cefpirome, colistin, daptomycin, ertapenem, meropenem, teicoplanin, tigecycline and vancomycin against aerobic bacterial pathogens isolated from patients with nosocomial infections These nine antimicrobial agents are all used to treat nosocomial infections in Taiwan.

METHODS

In a prior study, aerobic and facultative bacteria isolated between January 2, 2004 and June 30, 2005 from blood, sputum, urine, pus, pleural fluid and cerebrospinal fluid of patients with nosocomial infections at Keelung Chang Gung Memorial Hospital were collected consecutively and identified using standard procedures, and the study results were reported.[14] Clinically significant aerobic bacterial isolates were collected and stored in tryptic soy broth and frozen at –70°C. Nosocomial infections were defined according to the criteria for noscomial infections set by the Centers for Disease Control in 1988.[15] For our present study, we utilized the bacteria collected and stored in this prior study.

Antimicrobial susceptibility was evaluated by Etest according to the guidelines of Clinical and Laboratory Standards Institute (CLSI) Document M7-A7 2006[16] and AB Biodisk, Solna, Sweden. For tigecycline inhibition of *A. baumannii*, the broth microdilution method was used.[17] The MICs of nine antimicrobial agents, ampicillin/sulbactam (Pfizer, New York City, NY, U.S.A.), cefpirome (Sanofi-Aventis, Paris, France), colistin (Parkdale Pharmaceuticals, Rochester, MI, U.S.A.), daptomycin (Cubist Pharmaceuticals, Boston, MA, U.S.A.), ertapenem (MSD, Whitehouse Station, New Jersey, U.S.A.), meropenem (Sumitomo Pharmaceuticals, Osaka, Japan), teicoplanin (Sanofi-Aventis, Paris, France), tigecycline (MSD, Whitehouse Station, New Jersey, U.S.A.) and vancomycin (Eli Lilly, Indianapolis, IN, U.S.A.) for the bacterial isolates were determined by Etest (AB Biodisk, Solna, Sweden). Susceptibility testing with daptomycin, teicoplanin and vancomycin was performed only with gram-positive bacteria. The tested antibiotics and their concentration ranges were ampicillin/sulbactam (0.016-256/0.008-128 μg/ml), cefpirome (0.016-256 μg/ml), colistin (0.064-1024 μg/ml), daptomycin (0.016-256 μg/ml), ertapenem (0.002-32 μg/ml), meropenem (0.002-32 μg/ml), teicoplanin (0.016-256 μg/ml), tigecycline (0.016-256 μg/ml), and vancomycin (0.016-256 μg/ml). In the antibiotic susceptibility testing with Etest, blood agar (BBL, U.S.A.) was used for streptococci, Haemophilus Test

Medium agar (BBL, U.S.A.) for *Hemophilus influenzae*, and Mueller-Hinton agar (BBL, U.S.A.) for the other tested organisms. The MICs were read where the inhibition ellipse intersected the scale on the strip after incubation at 35° or 24 hours. For quality control, standard control strains were included with each test run. The following organisms with acceptable MIC (μg/ml) limits were included as control strains according to the following standards from CLSI document M100-S19 released in January 2009: *S. aureus* ATCC 29213 (0.25-1 for daptomycin, 0.06-0.25 for ertapenem, 0.03-0.12 for meropenem, 0.03-0.25 for tigecycline), *E. coli*. ATCC 25922 (2/1-8/4 for ampicillin/ sulbactam, 0.25-1 for colistin, 0.004-0.015 for ertapenem, 0.008-0.06 for meropenem, 0.03-0.25 for tigecycline), *P. aeruginosa* ATCC 27853 (0.25-2 for colistin, 2-8 for ertapenem, 0.25-1 for meropenem), *Streptococcus pneumoniae* ATCC 49619 (0.06-0.5 for daptomycin, 0.03-0.25 for ertapenem, 0.06-0.25 for meropenem, 0.015-0.12 for tigecycline), *Enterococcus faecalis* ATCC 29212 (1-4 for daptomycin, 4-16 for ertapenem, 2-8 for meropenem, 0.03-0.12 for tigecycline).

According to CLSI M100-S19 released in January 2009 and recent literature,[18-20] anitbiotics active against Enterobacteriaceae, non-fermenting Gram-negative bacilli and staphylococci and their susceptible (S), intermediate (I) and resistant (R) breakpoints (μg/ml) are ampicillin/sulbactam (S ≦ 8/4; I = 16/8; R ≧ 32/16), cefpirome (S ≦ 8; I = 16; R ≧ 32; the breakpoints of cefepime were used for cefpirome), colistin (S ≦ 2; R ≧ 4), daptomycin (S ≦ 1), ertapenem (S ≦ 2; I = 4; R ≧ 8), meropenem (S ≦ 4; I = 8; R ≧ 16), and tigecycline (S ≦ 2; the proposed breakpoint from the US Food and Drug Administration [FDA]).[21] Other antibiotics active against staphylococci and their MIC (μg/ml) breakpoints are oxacillin (S ≦ 2; R ≧ 4), teicoplanin (S ≦ 8; I = 16; R ≧ 32), and vancomycin (S ≦ 2; I = 4-8; R ≧ 16). The MIC breakpoints of vancomycin active against coagulase-negative staphylococci were S ≦ 4; I = 8-16; R ≧ 32.[20] According to the CLSI, all oxacillin-resistant staphylococci are considered resistant to beta-lactam. The antibiotics active against streptococci and their MIC breakpoints are cefpirome (S ≦ 1; I = 2; R ≧ 4; breakpoints of cefepime were used for cefpirome), daptomycin (S ≦ 1), ertapenem (S ≦ 1; I = 2; R ≧ 4), meropenem (S ≦ 0.25; I = 0.5; R ≧ 1 resistan), oxacillin (S ≦ 2; R ≧ 4 resistant), teicoplanin (S ≦ 2), tigecycline (S ≦ 2 sensitive; proposed breakpoint from the FDA),[21] and vancomycin (S ≦ 1).[18,20] Antibiotics active against enterococci and their MIC breakpoints are ampicillin/sulbactam (S ≦ 8/4; R ≧ 16/8), daptomycin (S ≦ 4), ertapenem (S ≦ 2; I = 4; R ≧ 8), meropenem (S ≦ 4; I = 8; R ≧ 16), teicoplanin (S ≦ 8; I = 16; R ≧ 32), tigecycline (S ≦ 2; proposed breakpoint from the FDA),[21] and vancomycin (S ≦ 4; I = 8-16 R ≧ 32).[18,20] Antibiotics active against Hemophilus spp. and their MIC breakpoints are ampicillin/sulbactam (S ≦ 2/1; R ≧ 4/2), cefpirome (S ≦ 2), ertapenem (S ≦ 0.5), meropenem (S ≦ 0.5), and tigecycline (S ≦ 2; proposed breakpoint from the FDA).[21] MDR-*Acinetobacter baumannii* was defined as an *Acinetobacter baumannii* isolate that is resistant to aminoglycosides, β-lactamse inhibitors, carbapenems, cephalosporins and quinolones, but not to colistin and tigecycline. MDR-*P. aeruginosa* was defined as a *P. aeruginosa* isolate resistant to aminoglycosides, β-lactamse inhibitors, carbapenems, cephalosporins, quinolones and tigecycline, but not to colistin. MDR-Enterobactericeae was defined as an Enterobactericeae spp. isolate resistant to aminoglycosides, β-lactamse inhibitors, carbapenems, cephalosporins and quinolones, but not to colistin and tigecycline.

RESULTS

A total of 208 isolates subjected to susceptibility testing were sampled from a variety of nosocomial infections, which included bacteremia (n = 142), urinary tract infections (n = 40), pneumonia (n = 8), wound infections (n = 5), meningitis (n = 3), pleural infection (n = 1), central venous catheter wound infection (n = 1) and subcutaneous soft tissue infection (n = 1). Most (140/208, 67%) of the isolates were facultative Gram-negative bacilli. The most common single organism was *S. sureus,* which accounted for 47/208, 22.6% of the total. Antimicrobial activities of all nine antimicrobial agents against all bacteria tested are shown in the Table. Among the nine antimicrobial agents, ampicillin/sulbactam, ertapenem, meropenem, teicoplanin, tigecycline and vancomycin were active (16/16, 100%) against oxacillin-sensitive *S. aureus* (Table). All 31 ORSA isolates were susceptible to teicoplanin and vancomycin (31/31, 100%) but the

MICs of vancomycin for all 31 ORSA isolates were ≧ 1 μg/ml (Table). Sixteen of the 31 ORSA isolates were sensitive to daptomycin (16/31, 51.6%) according to the breakpoint ≦ 1 μg/ml for daptomycin. Ampicillin/sulbactam, teicoplanin and vancomycin were 100% active (4/4, 100%) against coagulase(-) staphylococci. The antimicrobial agents with the in-vitro inhibition of Enterococcus spp. were ampicillin/sulbactam 8/10, 80%; teicoplanin 10/10, 100%; tigecycline 8/10, 80%; and vancomycin 10/10, 100% (Table). Streptococcus spp, which infrequently cause nosocomial infections,[22] were 100% susceptible to ampicillin/sulbactam, teicoplanin and tigecycline (8/8, 100%). Of the 11 isolates of. *A. baumannii* that were not MDR, 10 isolates (10/11, 91%) were susceptible to colistin and all 11 isolates (11/11, 100%) were susceptible to meropenem and tigecycline. Of the 21 isolates of MDR-*A. baumannii*, 19 isolates (19/21, 90%) were sensitive to colistin and 18 isolates (18/21, 86%) were sensitive to tigecycline. Of the 22 isolates of *E. coli* with ESBL, the antimicrobial agents with the highest susceptible rates were colistin (20/22, 91%), ertapenem (21/22, 96%), meropenem and tigecycline (22/22, 100%)(Table). However, of the 15 isolates of *E. coli* without ESBL were susceptible to meropenem (14/15, 93%), and 13 isolates to 14 isolates tigecycline (13/15, 87%). The 3 isolates of Enterobacter cloacae with ESBL were 100% susceptible (3/3, 100%) to colistin and meropenem. However, of the 3 isolates of *E. cloacae* without ESBL, all isolates were susceptible to cefpirome and meropenem (3/3, 100%), and 2 isolates to colistin, ertapenem and tigecycline (2/3, 66%). The 16 *K. pneumoniae* isolates with ESBL were 100% susceptible (16/16, 100%) to colistin, ertapenem and meropenem while 14 isolates were susceptible to tigecycline (14/16, 87%). The susceptibility of *K. pneumoniae* without ESBL to ampicillin/sulbactam, cefpirome, colistin, ertapenem, meropenem, tigecycline was 13/15 (87%), 15/15 (100%), 13/15 (87%), 15/15 (100%), 15/15 (100%), and 13/15 (87%) respectively. The five isolates of *Serratia marcescens* were 100% susceptible (5/5, 100%) to ertapenem, meropenem and tigecycline. Six of the 11 isolates of *P. aeruginosa* were susceptible to colistin (6/11, 55%) and all isolates were susceptible to meropenem (11/11, 100%). All isolates of *P. aeruginosa* were resistant to tigecycline (Table).

Table In Vitro Activity of Nine Antibiotics against 208 Isolates from Nosocomial Infections

Organism (n)	Antibiotic	MIC (μg/ml)			S	I	R
		Range	MIC50	MIC90	%	%	%
Staphylococcus aureus OSSA (16)	ampicillin/sulbactam	0.38-6	2	4	100	0	0
	cefpirome	2-256	6	256	86.7	0	13.3
	colistin	12-512	256	512	0	0	100
	daptomycin	0.125-2	1	1.5	75	0	25
	ertapenem	0.038-1	0.38	1	100	0	0
	meropenem	0.094-0.25	0.19	0.19	100	0	0
	oxacillin	0.25-1.5	0.5	1	100	0	0
	teicoplanin	0.75-2	1.5	1.5	100	0	0
	tigecycline	0.047-0.25	0.125	0.19	100	0	0
	vancomycin	0.75-1.5	1.5	1.5	100	0	0
Staphylococcus aureus ORSA (31)	ampicillin/sulbactam	1.5-86	16	32	25.8	51.6	22.6
	cefpirome	2-256	128	256	0	3.2	96.8
	colistin	32-1024	512	1024	0	0	100
	daptomycin	0.75-2	1	2	48.4	0	51.6
	ertapenem	1-32	32	32	6.5	6.5	87
	meropenem	0.064-32	32	32	6.5	6.5	87
	oxacillin	4-256	256	256	0	0	100
	teicoplanin	1.5-6	2	4	100	0	0
	tigecycline	0.032-16	0.125	0.75	96.8	0	3.2
	vancomycin	1-2	1.5	2	100	0	0

Table In Vitro Activity of Nine Antibiotics against 208 Isolates from Nosocomial Infections (Continued)

Organism (n)	Antibiotic	MIC (μg/ml)			S	I	R
		Range	MIC50	MIC90	%	%	%
Coag.(-) staphylococci (4)	ampicillin/sulbactam	0.19-4	0.25	4	100	0	0
	cefpirome	0.125-12	1	12	75	25	0
	colistin	6-1024	16	1024	0	0	100
	daptomycin	1-3	1	3	50	0	50
	ertapenem	0.38-32	0.38	32	50	0	50
	teicoplanin	1-2	1.5	2	100	0	0
	tigecycline	0.064-1.5	0.5	1.5	100	0	0
	vancomycin	1.5-2	1.5	2	100	0	0
Enterococcus spp.(10)	ampicillin/sulbactam	0.032-256	2	32	80	0	20
	cefpirome	0.19-256	256	256	10	0	90
	colistin	0.38-1024	1024	1024	10	0	90
	daptomycin	1.5-3	2	3	100	0	0
	ertapenem	0.032-32	12	32	30	0	70
	teicoplanin	2-8	4	6	100	0	0
	tigecycline	0.064-1.5	0.5	1.5	100	0	0
	vancomycin	1-6	2	4	100	0	0
Streptococcus spp.(8)	ampicillin/sulbactam	0.064-1	0.32	1	100	0	0
	cefpirome	0.125-256	256	256	33		67
	colistin	12-1024	1024	1024	0	0	100
	daptomycin	0.125-12	0.25	0.75	75	0	25
	ertapenem	0.094-0.19	0.64	0.125	100	0	0
	teicoplanin	2	2	2	100	0	0
	tigecycline	0.094-0.64	0.19	0.64	100	0	0
	vancomycin	1-1.5	1	1.5	83	0	17
Acinetobacter baumannii-MDR (21)	ampicillin/sulbactam	3-256	16	64	14.3	66.7	19
	cefpirome	8-256	256	256	6.25	6.25	87.5
	colistin	0.25-1024	0.75	1.5	90.5	0	9.5
	ertapenem	8-32	32	32	0	0	100
	meropenem	4-256	32	256	6.25	0	93.7
	tigecycline	0.032-0.5	0.125	0.5	100	0	0
Acinetobacter baumannii non-MDR (11)	ampicillin/sulbactam	1-24	2	16	63.6	27.3	9.1
	cefpirome	8-256	24	256	20	27.3	52.7
	colistin	0.38-1024	0.75	1	90.9	0	9.1
	ertapenem	1.5-12	3	8	27.3	45.4	27.3
	meropenem	0.064-2	0.38	1	100	0	0
	tigecycline	0.032-1	0.125	1	100	0	0
Escherichia coli-ESBL (22)	ampicillin/sulbactam	12-96	32	64	0	43.5	56.5
	cefpirome	4-256	64	256	36	13	51
	colistin	0.25-1024	0.75	2	91.3	0	8.7
	ertapenem	0.032-32	0.19	0.5	91.3	0	8.7
	meropenem	0.032-0.47	0.064	0.125	100	0	0
	tigecycline	0.032	0.5	2	100	0	0
Escherichia coli non-ESBL (15)	ampicillin/sulbactam	0.25-128	8	64	60	26.7	13.3
	cefpirome	0.016-256	0.094	256	66.7	13.3	20
	colistin	0.19-1024	1	64	80	0	20

Table In Vitro Activity of Nine Antibiotics against 208 Isolates from Nosocomial Infections (Continued)

Organism (n)	Antibiotic	MIC (μg/ml)			S	I	R
		Range	MIC50	MIC90	%	%	%
	ertapenem	0.012-32	0.047	6	73	0	27
	meropenem	0.023-12	0.047	2	93	0	7
	tigecycline	0.094-6	0.25	6	80	0	20
Klebsiella pneumoniae-ESBL (16)	ampicillin/sulbactam	16-256	84	256	0	12.5	87.5
	cefpirome	4-256	256	256	6	0	94
	colistin	0.25-2	0.75	1	100	0	0
	ertapenem	0.147-1	0.25	0.75	100	0	0
	meropenem	0.032-0.64	0.094	0.125	100	0	0
	tigecycline	0.75-6	1.5	4	81	0	19
Klebsiella pneumonia non-ESBL (15)	ampicillin/sulbactam	2-64	4	16	86.7	6.7	6.7
	cefpirome	0.023-24	0.064	0.125	93.3	0	6.7
	colistin	0.38-1024	1	1024	86.7	0	13.3
	ertapenem	0.012-2	0.047	0.23	100	0	0
	meropenem	0.032-0.47	0.047	0.125	100	0	0
	tigecycline	0.032-24	0.75	12	86.7	x	x
Enterobacter cloacae-ESBL (3)	ampicillin/sulbactam	64-256	128	256	0	0	100
	cefpirome	48-256	256	256	0	0	100
	colistin	0375-1	1	1	100	0	0
	ertapenem	0.5-8	4	8	33.3	33.3	33.3
	meropenem	0.094-1	0.25	1	100	0	0
	tigecycline	1.5-8	4	8	33.3	0	66.7
Enterobacter cloacae non-ESBL (3)	ampicillin/sulbactam	4-256	16	256	33.3	0	66.7
	cefpirome	0.038-8	0.094	8	100	0	0
	colistin	0.25-4	2	4	66.7	0	33.3
	ertapenem	0.016-32	0.19	32	66.7	0	33.3
	meropenem	0.064-0.47	0.19	0.47	100	0	0
	tigecycline	1-3	1.5	3	66	x	x
Serratia marcescens (5)	ampicillin/sulbactam	12-256	128	256	20	0	80
	cefpirome	0.064-256	256	256	50	0	50
	colistin	24-1024	128	256	0	0	100
	ertapenem	0.032-0.125	0.064	0.125	100	0	0
	meropenem	0.047-0.125	0.094	0.094	100	0	0
	tigecycline	0.75-2	1	2	100	0	0
Pseudomonas aeruginosa (11)	ampicillin/sulbactam	128-256	256	256	0	0	100
	cefpirome	4-256	16	256	36	18.2	45.8
	colistin	1.5-8	3	8	54.5	0	45.5
	ertapenem	1-32	16	32	18.2	18.2	63.6
	meropenem	0.094-1	0.25	0.5	100	0	0
	tigecycline	8-256	24	256	0	x	x
Miscellaneous Enterobacteriaceae & Aeromonadaceae (10)	ampicillin/sulbactam	0.38-256	4	256	60	20	20
	cefpirome	0.016-256	0.5	256	40	20	40
	colistin	0.38-1024	2	1024	50	0	50
	ertapenem	0.008-0.25	0.032	0.125	100	0	0
	meropenem	0.023-0.25	0.125	0.25	100	0	0

Table In Vitro Activity of Nine Antibiotics against 208 Isolates from Nosocomial Infections (Continued)

Organism (n)	Antibiotic	MIC (μg/ml)			S	I	R
		Range	MIC50	MIC90	%	%	%
	tigecycline	0.125-32	1	12	70	x	x
Miscellaneous Non-fermenting Gram-negative bacilli (5)	ampicillin/sulbactam	24-256	96	256	0	0	100
	cefpirome	256	256	256	0	0	100
	colistin	1.5-1024	32	1024	20.0	0	80.0
	ertapenem	3-32	12	32	0	20.0	80.0
	meropenem	0.94-32	32	32	20.0	20.0	60.0
	tigecycline	0.25-96	1.5	96	20.0	0	80.0
Hemophilus influenzae (1)	ampicillin/sulbactam	0.094	0.094	0.094	100	0	0
	cefpirome	0.38	0.38	0.38	100	0	0
	colistin	3	3	3	0		
	ertapenem	0.25	0.25	0.25	100	0	0
	meropenem	0.064	0.064	0.064	100	0	0
	tigecycline	0.047	0.047	0.047	100	0	0
Corynebacterium jeikeium (1)	ampicillin/sulbactam	0.38	0.38	0.38	100	0	0
	cefpirome	256	256	256	0	0	100
	colistin	12	12	12	0	0	100
	daptomycin	0.125	0.125	0.125	100	0	0
	ertapenem	0.038	0.038	0.038	100	0	0
	tigecycline	0.047	0.047	0.047	100	0	0

Abbreviations: OSSA: oxacillin-susceptible *S. aureus*; ORSA: oxacillin-resistant *S. aureus*; MDR: multiple-drug-resistant; ESBL: extended-spectrum beta-lactamase; S: sensitive; I: intermediate; R: resistant.

Enterococcus spp. include 8 *Enterococcus faecalis*.

Streptococcus spp. include 1 beta-hemolytic Streptococcus Gr. B, 1 *Streptococcus bovis*, 1 *Streptococcus mitis*, 1 *Streptococcus salivarius*, 1 *Streptococcus sanguis*, 1 *Streptococcus viridans*.

Miscellaneous Enterobacteriaceae & Aeromonadaceae include 1 *Aeromonas hydrophilia*, 1 *Citrobacter amalonaticus*, 1 *Enterobacter aerogenes*, 1 *Enterobacter agglomerans*, 1 *Morganella morganii*, 1 *Proteus mirabilis*, 1 *Providencia alcalifaciens*, 2 *Salmonella enteritidis*, 1 *Serratia liquefaciens*.

Miscellaneous non-fermenters include 1 *Acinetobacter hemolyticus*, 1 *Chryseobacterium meningosepticum*, 1 *Alcaligenes faecalis*, 2 *Stenotrophomonas maltophilia*.

DISCUSSION

Although all 31 ORSA isolates were sensitive to teicoplanin, and vancomycin (31/31, 100%), the MICs of vancomycin and teicoplanin for all 31 ORSA isolates were ≧ 1 μg/ml and ≧ 1.5 μg/ml respectively (Table). This result indicates that ORSA has reduced susceptibility to vancomycin and teicoplanin since the MICs of vancomycin and teicoplanin for ORSA isolates were usually ≦ 1 μg/ml in our hospital in the past (unpublished data). Other antibiotics such as daptomycin or linezolid or combination therapy may be needed in severe infections caused by ORSA.[23]

A. baumannii which is intrinsically resistant to multiple antibiotics is a frequent pathogen in nosocomial infections. Nineteen of the 21 isolates of MDR-*A. baumannii* were susceptible to colistin and 18 to tigecycline. This is consistent with prior reports.[6,7,24-26] For *E. coli* with ESBL, the antimicrobial agents with the highest inhibitory rates were colistin, ertapenem, meropenem and tigecycline, consistent with previous reports.[27-29] For *Enterobacter cloacae* with ESBL, colistin and meropenem had the highest inhibitory rates. *K. pneumoniae* isolates with ESBL were 100% susceptible (16/16, 100%) to colistin, ertapenem and meropenem, followed by tigecycline (13/16, 81%), compatible with prior reports.[13] Six of

the 11 isolates of *P. aeruginosa* were susceptible to colistin and all isolates were susceptible to meropenem (Table).

Although MDR-*A. baumannii* in nosocomial infections appears increasingly resistant to levofloxacin, ciprofloxacin, ceftazidime, cefepime, imipenem and tazobactam/piperacillin in Taiwan,[11,12] there are still effective antimicrobial agents. MDR-*A. baumannii* is usually susceptible to colistin and tigecycline in Taiwan according to the results of this study. ORSA is usually susceptible to vancomycin, teicoplanin or daptomycin. However, in this study, the MICs of vancomycin, teicoplanin (≧ 1 μg/ml, Table) and daptomycin (≧ 0.75 μg/ml, Table) for ORSA have increased and indicate that ORSA has reduced susceptibility to these antibiotics. This is consistent with prior reports.[10-12] The high resistance rate of ORSA to daptomycin found in this study (51.6%, Table) may indicate that these hospital-acquired ORSA isolates are multi-drug-resistant and can develop resistance to any new antimicrobial agent after usage for a certain period. Further study is needed to evaluate the clinical and in vitro efficacy of high dose daptomycin and combination therapy for ORSA infections with reduced susceptibility to these antibiotics, especially in severe infections before the antibiotic susceptibility profile of the culprit ORSA is available. For MDR-*P. aeruginosa*, further study is needed.

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北台灣一醫院九種現今抗生素對院內感染菌株抗菌效力之比較

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背 景： 這個研究主要在比較 ampicillin/sulbactam, cefpirome, colistin, daptomycin, ertapenem, meropenem, teicoplanin, tigecycline, vancomycin 對院內感染菌株之抗菌效力。

方 法： 本研究使用 Etest 方法，來測試抗生素的抗菌效力，Tigecycline 的感受性試驗，則使用 broth microdilution 方法。

結 果： 大部份的菌株 (140/208, 67%) 是革蘭氏陰性桿菌。在 31 株 oxacillin- 抗藥性金黃色葡萄球菌 (ORSA) 之中，16 株對 daptomycin 有感受性 (16/31, 51.6%；最低抑制濃度 MIC ≦ 1 μg/ml 定爲有感受性)。全部 31 株 ORSA 均對 teicoplanin 及 vancomycin 有感受性，但 vancomycin 對全部 31 株 ORSA 的 MIC 均 ≧1 μg/ml。在 21 株多種藥物抗藥性 multiple-drug-resistant (MDR) 之鮑氏不動桿菌 *Acinetobacter baumannii*，19 株 (19/21, 90%) 對 colistin 有感受性，18 株 (18/21, 86%) 對 tigecycline 有感受性。在 22 株帶廣效性 beta-lactamase (ESBL) 大腸桿菌 *E. coli*，抗菌效力最高的是 colistin (20/22, 91%)，ertapenem (21/22, 96%)，meropenem 及 tigecycline (22/22, 100%)。在 11 株綠膿桿菌 *P. aeruginosa*，6 株對 colistin 有感受性 (6/11, 55 %)，全部 11 株綠膿桿菌均對 meropenem 有感受性 (11/11, 100%)，但均對 tigecycline 有抗藥性。

結 論： 根據本研究的結果，多種藥物抗藥性鮑氏不動桿菌 MDR-*Acinetobacter baumannii* 引起之院內感染，colistin 及 tigecycline 會有效。有關 ORSA 引起之院內感染，ORSA 對 vancomycin, teicoplanin 及 daptomycin 的感受程度已下降。有關多種藥物抗藥性綠膿桿菌 MDR-*P. aeruginosa*，須要更多的研究才能確定有效之抗生素治療。

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關鍵詞：抗菌效力，九種現行抗生素，院內感染菌株

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