E-2082

The First Nationwide Surveillance of Bacterial Pathogens in Adult Respiratory Tract Infections (RTI) Conducted by Japanese Society of Chemotherapy (JSC) : Studies on Susceptibility of *Pseudomonas aeruginosa*

Y. NIKI [1], S. KOHNO [1], N. AOKI [1], A. WATANABE [1], J. SATO [1], M. YAGISAWA [2], H. HANAKI [2];[1]JSC Surveillance Committee, Tokyo, Japan, [2]The Kitasato Inst., Tokyo, Japan.

Abstract

A total of 143 *P.aeruginosa* was collected from well-diagnosed adult RTI patients in the JSC surveillance conducted during the period of January – April 2006.

Susceptibilities of the isolates from sputum or specimens obtained by TAA or bronchoscopy to 21 antibacterial agents including 5 quinolones [QL; ciprofloxacin (CPFX), levofloxacin (LVFX), gatifloxacin (GFLX), tosufloxacin (TFLX) and pazufloxacin (PZFX)] were determined according to the CLSI micro-broth dilution standards.

The isolates were stratified into those from patients of community- or hospital-acquired infections, without (NCTT) or with (CCT) catheter (ureteral, venous, bronchial and others), in age and under diagnosis.

Unexpected difference between NCTT (n=101) and CCT (n=42) was noted; 20 (19.8%) of NCCT were QL-resistant (QLR) while 1 (2.4%) was QLR in CTT. In addition, highly quinolone-resistant strain (HR; MIC ≥ 128μg/mL) was noted in 7 (6.9%) of NTTC while no HR was found in CTT. No difference in QLR was noted between isolates under the other stratifications. No particular resistant tendency against other class of agents was observed under stratifications.

QL	NCTT (n = 101)			CTT (n = 42)		
	MIC_{50}	MIC_{90}	QLR (%)	MIC_{50}	MIC_{90}	QLR (%)
CPFX	0.25	16	16 (15.8)	0.125	0.5	1 (2.4)
LVFX	1.0	32	20 (19.8)	1.0	2.0	1 (2.4)
GFLX	1.0	32	18 (17.8)	1.0	4.0	0 (0.0)
TFLX	0.25	≥ 32	17 (16.8)	0.25	1.0	0 (0.0)
PZFX	0.5	16	18 (17.8)	0.5	2.0	0 (0.0)

It is notable that NCTT tend to be resistant to QL including highly resistant ones. It might be caused by over usage of QL in community-acquired infections.

Background

In order to investigate trends and transition of bacterial pathogens and emergence of resistance among them, Japanese Society of Chemotherapy (JSC) established a nationwide surveillance network in 2006.

The first survey was conducted in adult respiratory tract infections (RTI) during the period from January to April, 2006 under the cooperation of 32 medical institutions throughout Japan.

To keep the quality of surveillance high, collection of bacterial strains were limited to clinically relevant species such as *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Haemophilus influenzae*, *Moraxella catarralis*, *Klebsiella pneumoniae* and *P.seudomonas aeruginosa* and to those isolated as causative bacteria from well-diagnosed patients.

The electronic uniform data sheet on each isolate facilitates quality assurance of diagnosis (with symptoms and signs, laboratory tests, radiological imaging) and pathogen (collection / nature / volume of sputum, Gram staining and phagocytosis, quantitative culture, species identification).

The data sheet also enables us to stratify these pathogens under background and setting of patients (gender, age, diagnosis, underlying disease, out- / in-patient, with / without catheter) from whom they were isolated.

Materials & Methods

・A total of 924 strains had been received at the central laboratory, the Research Center for Anti-infective Drugs of the Kitasato Institute, in ideal condition and, after re-identification and cultivation, 887 evaluable strains consisted of 205 *S.aureus*, 200 *S. pneumoniae*, 9 *S. pyogenes*, 165 *H. influenzae*, 91 *M. catarralis*, 74 *K. pneumoniae* and 143 *P.aeruginosa* were employed to antibacterial susceptibility testing.

・Susceptibility testing was performed according to the CLSI (formerly NCCLS) standards M7-A7 for micro-broth dilution method. In brief, cation-adjusted Mueller- Hinton broth (25mg/L Ca++ and 12.5mg/L Mg++; CA-MH broth) was used to measure MIC against *S.aureus, M.catarrhalis, K.pneumoniae* and *P.aeruginosa*. Against *S.pneumoniae* and *S.pyogenes,* CA-MH broth was added with lysed horse blood at 2.5 to 5% v/v. Against *H.influenzae*, *Haemophilus* Test Medium (HTM) was used.

・ Test organism solution was adjusted to final concentration of $5x10^4$ CFU/well, and inoculated to respective CA-MH broth to make a final volume of 0.1 ± 0.02 mL. It was poured into a well on a microplate where a serially diluted freeze-dried test agent was placed, and MIC was determined by MIC 2000 system (Eiken Kagaku Co., Ltd., Tokyo).

・Accuracy of determination for minimum inhibitory concentration (MIC) of antibacterial agents was controlled according to the recommendations of CLSI standards using the respective control strains.

Results & Discussion

Almost of all analyses on these 887 strains under various stratifications, Fig.1, gave reasonable results reflective of the general tendency in emergence and spread of resistance to variety of antibacterial agents except for two unexpected facts.

One is the tendency of methicillin-sensitive *S.aureus* (MSSA) to become resistance to fluoroquinolones (to be published elsewhere). The other is that *P.aeruginosa* strains isolated from patients without catheterization tend to become resistant to fluoroquinolones but those from patients with catheter remain susceptible (Fig. 2, Table1 & 2).

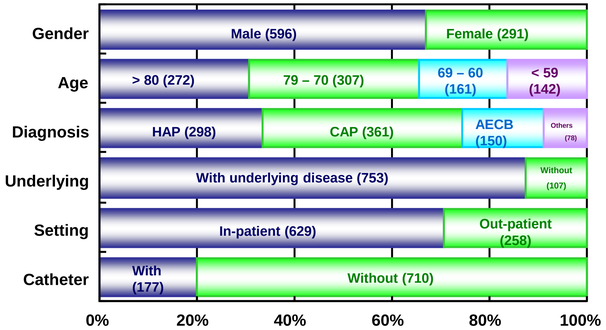

Fig. 1 Stratification of all strains (n = 887) in the study

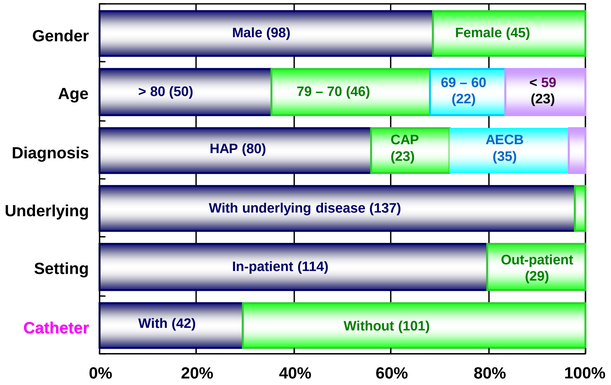

Fig. 2 Stratification of *P.aeruginosa* strains (n = 143)

Antibacterial agent	with catheter; n = 42			without catheter; n = 101		
	MIC (μg/mL)			MIC (μg/mL)		
	Range	50%	90%	Range	50%	90%
Piperacillin	2 - ≥256	4	128	0.25 - ≥256	4	128
Tazobactam/ Piperacillin	2 - ≥256	4	128	≤0.06 - ≥256	4	64
Caftazidime	0.5 - 32	2	32	≤0.06 - ≥128	2	16
Ceftriaxone	4 - ≥256	32	≥256	1 - ≥256	64	≥256
Cefepime	0.5 - 16	2	8	0.125 - ≥256	2	16
Cefozopran	0.25 - 16	1	8	0.125 - ≥256	1	16
Aztreonam	1 - 64	4	16	≤0.06 - ≥256	4	32
Imipenem	0.25 - ≥128	2	16	≤0.06 - ≥128	2	16
Panipenem	0.125 - ≥256	4	32	0.125 - ≥256	4	16
Meropenem	≤0.06 - 32	1	8	≤0.06 - ≥256	1	16
Biapenem	0.125 - 128	1	8	≤0.06 - ≥256	0.5	8
Doripenem	≤0.06 - ≥32	0.5	2	≤0.06 - ≥32	0.5	8
Gentamicin	0.125 - ≥256	0.5	2	≤0.06 - ≥256	0.5	4
Amikacin	0.5 - ≥256	1	4	0.25 - 64	2	4
Arbekacin	0.25 - ≥256	0.5	2	0.125 - 8	1	4
Minocycline	0.5 - ≥256	8	64	0.125 - ≥256	16	≥256
Ciprofloxacin	≤0.06 - 4	0.125	0.5	≤0.06 - 128	0.25	16
Levofloxacin	0.5 - 16	1	2	≤0.06 - ≥256	1	32
Tosufloxacin	≤0.06 - 4	0.25	1	≤0.06 - ≥32	0.25	≥32
Gatifloxacin	0.125 - 4	1	4	≤0.06 - ≥256	1	32
Pazufloxacin	≤0.06 - 4	0.5	2	≤0.06 - ≥256	0.5	16

Table 1 Susceptibility of *P.aeruginosa* strains stratified under catheterization

Fluoroquinolone antibacterial	with catheter; n = 42		without catheter; n = 101	
	MIC_{90} (μg/mL)	Resistant strain (%)	MIC_{90} (μg/mL)	Resistant strain (%)
Ciprofloxacin	0.5	1 (2.4)	16	16 (15.8)
Levofloxacin	2.0	1 (2.4)	32	20 (19.8)
Gatifloxacin	4.0	0 (0.0)	32	18 (17.8)
Tosufloxacin	1.0	0 (0.0)	≥32	17 (16.8)
Pazufloxacin	2.0	0 (0.0)	16	18 (17.8)

Table 2 Susceptibility of *P.aeruginosa* to fluoroquinolone antibacterials stratified under catheterization

FLQs	HAP (n = 20)		CAP (n = 50)		AECB (n = 28)	
	MIC_{90} (μg/mL)	Resistance (%)	MIC_{90} (μg/mL)	Resistance (%)	MIC_{90} (μg/mL)	Resistance (%)
CPFX	2.0	10.0	32	22.0	8.0	10.7
LVFX	16	25.0	64	24.0	8.0	10.7
TFLX	2.0	10.0	≥32	24.0	8.0	10.7
GFLX	8.0	20.0	64	22.0	16	10.7
PZFX	8.0	15.0	64	26.0	4.0	7.1

Table 3 Fluoroquinolone-resistance of *P.aeruginosa* isolated from patients without catheter ; Analysis under stratification by type of infection

Conclusion

Acknowledgments

Cooperative Institutions ; Iwate Prefectural Central Hospital, Yamagata Saisei Hospital, Sanyudo Hospital, Fukushima Prefectural Aizu General Hospital, South Miyagi Medical Center, Japanese Red Cross Sendai Hospital, Sendai Kousei Hospital, Saka General Hospital, International Medical Center of Japan, National Hospital Organization Tokyo Medical Center, St. Luke's International Hospital, Tokyo Metropolitan Toshima Hospital, Kyorin University Hospital, Yamanashi Red Cross Hospital, Toyama Prefectural Central Hospital, Niigata University Medical & Dental Hospital, Niigata City General Hospital, Shinrakuen Hospital, Kawasaki Medical School Hospital, Hiroshima Prefectural Hospital, Shimonoseki City Central Hospital, Matsue Red Cross Hospital, Tottori University Hospital, Kagawa Medical University Hospital, Ehime Prefectural Central Hospital, Graduate School of Medical Sciences, Kyushu University, Kurume University School of Medicine, Oita University Faculty of Medicine, Saga Medical School Faculty of Medicine, Saga University, Saiseikai Kumamoto Hospital, Nagasaki University School of Medicine, Faculty of Medicine, University of the Ryukyus