

Comparison of Antibiotic Resistance of the Most Common Gram-negative Pathogens and *Staphylococcus aureus* Isolated from Patients with Urinary or Respiratory Tract Infections.

Huppertz K., Noll I., Wiedemann B. and the GENARS-group

Central Office of GENARS; Pharmaceutical Microbiology; University of Bonn; Meckenheimer Allee 168; 53115 Bonn; Germany

GENARS

ABSTRACT

Objectives Urinary tract infections (UTI) and respiratory tract infections (RTI) are the most common infections in hospitalised patients. As the most common pathogens for both kinds of infections are different, the antibiotics commonly used are not identical, resulting in different selection pressure. Therefore it should be expected that antimicrobial resistance of bacterial species isolated from both UTI and RTI should also be different. For those species which are causing infection in both sites we compare the incidence of resistance using the data of the German Network for Antimicrobial Resistance Surveillance (GENARS).

Methods In all laboratories involved in the GENARS-project, in the daily routine, susceptibility is measured by MIC determination. Once a week, for central evaluation these data are transmitted to the central office. Selection criteria for the query in a time frame of January 1st to November 30th in 2002 included all first isolates of a patient for the species common in both sites. Therefore the data of the typical kinds of patient-material of the respiratory tract (sputum, tracheal secretion, bronchial secretion, pleural puncture, material from pleural biopsy, pus, bronchioalveolar lavage) and the urinary tract (urine: mid stream, bag, catheter, puncture) were evaluated.

Results The number of cases evaluated with 80 – 2100 per species and antibiotic is quite high. Only those species have been evaluated which are common in both infection sites. Mainly nosocomial RTI's are included and not community acquired infections which are usually caused by *S. pneumoniae* and *H. influenzae*. Differences in the incidence of resistant strains (see table 2) are striking in some cases (9fold, Ciprofloxacin and *E. cloacae*) on a low level but may be significant also at a high level (3fold, 45% vs. 15% in *S. aureus* with Ciprofloxacin). Although these differences are significant, they seem not to be based on a principle.

Conclusions Antimicrobial resistance of the same bacterial species isolated from respiratory tract and from urinary tract of hospitalised patients in German university hospitals differs significantly. This might be due to the different therapeutical action for UTI and RTI. Thus for the calculated therapy not only local statistics in the epidemiology of resistance has to be considered but also the site of infection.

INTRODUCTION AND PURPOSE

In hospitalised patients urinary tract infections (UTI) and respiratory tract infections (RTI) are the most common infectious diseases (1, 2). The most common pathogens for both kinds of infections are different. That's why the antibiotics commonly used are not identical, resulting in different selection pressure. For bacterial strains isolated from both UTI and RTI it should therefore be expected that antimicrobial resistance of bacterial species should also be different. Antimicrobial therapy of UTI and RTI in hospitalised patients is mostly initiated empirically before the results of microbiological analysis are available. Therefore, there is a great need for surveillance at local, national and international level (3). In Germany, at national level the German Network for Antimicrobial Resistance Surveillance (GENARS) was founded which presently is funded by the German Federal Ministry of Health. Data of this project were used for comparing the incidence of resistance for those species which are causing infection in both sites, RTI and UTI.

METHODS

In Germany, presently six medical microbiology laboratories of university hospitals are taking part in the GENARS-project. These laboratories collect MIC-data on bacterial susceptibility against antibiotics for all species of clinical material identified in the laboratory routine. For central evaluation, each lab transmits its data to the central office to Bonn once a week.

For susceptibility testing four laboratories use the Micronaut®-system (Merlin GmbH; Bornheim), a microdilution procedure. In an automatic process 384-well microtiter-plates containing vacuum-dried antibiotics are filled with freshly inoculated Mueller-Hinton broth (Becton Dickinson/Difco; Heidelberg). All centres are using the same batch of kation adjusted Mueller-Hinton broth, which is reserved by the manufacturer for the study. According to DIN and NCCLS the inoculum contains approximately 5×10^5 CFU/ml (4, 6). The plates are read photometrically and results are transferred online for evaluation. One center uses a self prepared microdilution, another Vitek 2® (bioMérieux GmbH).

Project-Characteristics

1. identification of all clinical isolates to species-level
2. MIC-values for all isolates
3. continuous unlimited data flow
4. non-validated data for surveillance

At present 49 antibiotics are tested in the GENARS-project. According to the particular needs, resistance outbreaks and the market situation, the antibiotics can be exchanged. For quality assurance each lab tests QC strains regularly. MIC data from all isolates from clinical material enter the data collection. For early recognition of a development of antimicrobial resistance only non-validated MIC's are accepted (see frame "Project-Characteristics"). Due to the weekly data-transmissions to the central office the project may function as an early warning system.

Selection criteria for the query in a time frame of January 1st to November 30th in 2002 included all first isolates of a patient for the species common in both sites, UTI and RTI. Isolates were selected from all medical fields and all kinds of clinical wards (ICU's, general wards, acute day wards). Data on the typical kinds of patient-material of the respiratory tract (sputum, tracheal secretion, bronchial secretion, pleural puncture, material from pleural biopsy, pus, bronchioalveolar lavage) and the urinary tract (urine: mid stream, bag, catheter, puncture) were evaluated. The percentages of resistant strains were calculated according to DIN breakpoints (5).

RESULTS

In German GENARS-hospitals *S. aureus* and *E. coli* are the most common species in RTI's and UTI's, respectively, followed by *P. aeruginosa* (table 1). Differences in the percentage of resistance in strains of the same species isolated from RTI and UTI are obvious for many antibiotics (table 2). In general, resistance rates for UTI are higher in *E. cloacae*, *K. oxytoca* and *S. aureus*. For RTI, resistance rates are higher in *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *P. mirabilis*.

species	RTI		UTI	
	n	%	n	%
<i>S. aureus</i>	5860	4988	1100	2079
<i>P. aeruginosa</i>	612	283	139	230
<i>E. coli</i>	208	253	137	273
<i>K. pneumoniae</i>	119	233	137	282
<i>E. cloacae</i>	102	279	59	161
<i>K. oxytoca</i>	124	108	64	165
<i>P. mirabilis</i>	28	101	54	67

Table 1 Number of strains (n) for each species isolated from RTI and UTI. According to the different systems used for MIC determination and the amount of antibiotics measured, the number of strains is not a constant.

Antibiotic	<i>E. cloacae</i>		<i>E. coli</i>		<i>K. pneumoniae</i>		<i>K. oxytoca</i>		<i>P. aeruginosa</i>		<i>P. mirabilis</i>		<i>S. aureus</i>	
	R	%	R	%	R	%	R	%	R	%	R	%	R	%
Ampicillin	441	438	11	11	11	11	11	11	20	178	17	17	17	17
Piperacillin	32/19	24/24	14/18	14/18	18/11	17/13	19/16	19/16	11	14	11	11	11	11
Chloramphenicol	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cefiderol	8/15	12/18	14/19	14/19	11	12/22	18/20	18/20	11	14	11	11	11	11
Cefuroxime	11/12	14/18	19/19	19/19	11	12/14	11	11	11	14	11	11	11	11
Ciprofloxacin	3/11	9/14	4/12	5/11	13/11	13/11	13/11	13/11	11	14	11	11	11	11
Gentamicin	5/11	4/14	7/14	18/24	12/18	12/18	7/17	7/17	11	14	11	11	11	11
Plasmycin	21/16	20/24	22/16	22/16	11	11	11	11	11	14	11	11	11	11
Polymyxin	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Table 2 Percentage of resistance of bacteria isolated from UTI and RTI (UT/RTI). Bold letters indicate a difference between UTI and RTI of more than 5%. R = natural resistant = not done

To this rule one exception was found for *P. mirabilis* and Piperacillin proving a higher resistance rate for strains isolated from UTI's (fig. 2).

For antibiotics where the difference between UTI and RTI amounts to more than 5 %, the differences are pointed out in separate figures for each species (fig. 1 – fig. 7).

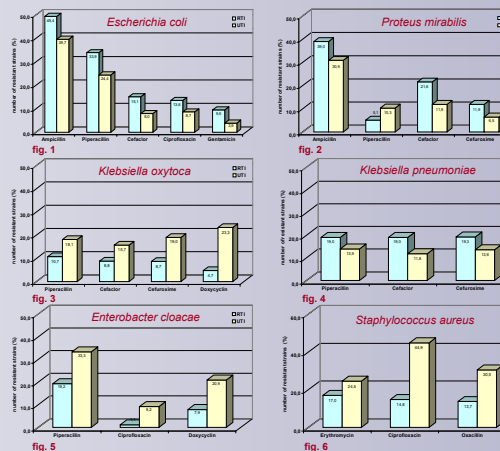


Fig. 1 – fig. 6 Percentages of resistant strains isolated from RTI (blue columns) and UTI (yellow columns) for different species and antibiotics. Only those antibiotics are chosen where the difference between RTI and UTI amounts to more than 5 %.

In *P. aeruginosa* the difference between RTI and UTI for Gentamicin is very high (fig. 7). Therefore MIC-distributions of strains isolated from UTI and RTI are compared (fig. 8). The modal value of the natural population peaks at 2 mg/l for strains from both, RTI and UTI. The number of strains from RTI with MIC's representing the natural sensitivity is lower, whereas strains with MIC's above 4 mg/l are more common.

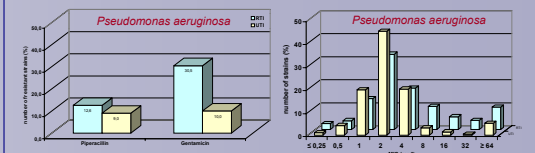


Fig. 7 Percentages of resistant strains of *P. aeruginosa* isolated from RTI (blue columns) and UTI (yellow columns) for Piperacillin and Gentamicin. Fig. 8 MIC-distributions of *P. aeruginosa* for Gentamicin from isolates from UTI (yellow columns) and RTI (blue columns).

CONCLUSIONS

In German university hospitals taking part in the GENARS-project, antimicrobial resistance of the same bacterial species isolated from the respiratory tract (RTI) and from the urinary tract (UTI) of hospitalised patients differs for many antibiotics examined. Differences between the resistance rates of strains from RTI and UTI depends on species and antibiotics selected and not on a common mechanism. The differences observed might be due to different therapeutical action. Thus, for the calculated therapy not only a general local statistic of the epidemiology of resistance has to be considered but also the site of infection.

REFERENCES

1. Stamm W.E., Hooton T.M. (1993). The management of urinary tract infection. *New England Journal of Medicine*; 329: 1328-1334.
2. Warren J.W., Abrutyn E., Hebel J.R., Johnson J.R., Schaeffer A.J., Stamm W.E. (1999). Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. *Clinical Infectious Diseases*; 29: 745-758.
3. Farrell D.J., Morrissey I., De Rubels D., Robbins M., Felmingham D. (2003). A UK Multicentre Study of the Antimicrobial Susceptibility of Bacterial Pathogens Causing Urinary Tract Infection. *Journal of Infection*; 46: 94-100.
4. National Committee of Clinical Laboratory Standards (2000). Methods for dilution of antimicrobial susceptibility tests for bacteria that grow aerobically. NCCLS document M7 – A5.
5. Deutsches Institut für Normung e.V. Empfindlichkeitsprüfung von mikrobiellen Krankheitserregern gegen Chemotherapeutika (2002). Teil 8: Mikrodilution – Allgemeine methodenspezifische Anforderungen. DIN 58940-8. Berlin: Beuth Verlag GmbH.
6. Deutsches Institut für Normung e.V. Empfindlichkeitsprüfung von mikrobiellen Krankheitserregern gegen Chemotherapeutika (2002). Teil 8: Mikrodilution – Spezielle Anforderungen an die Testung von nicht anspruchsvollen Bakterien. DIN 58940-81. Berlin: Beuth Verlag GmbH.