Ability of the Latin America Centers to Detect Antimicrobial Resistance Patterns: Experience of SENTRY Surveillance Antimicrobial Program – 1997-1999

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AMENDED ABSTRACT

The accuracy of antimicrobial susceptibility tests is a crucial step for the clinical management of patients with serious infections. They must be reliable and precise because they will guide the antimicrobial therapy. The principal aim of this study was to compare the susceptibility testing results performed by the SENTRY monitoring laboratory with those of reported by the Latin American participating medical centers (MC). A total of 6,616 bacterial isolates were tested by the reference broth microdilution at University of Iowa. The tests were performed and interpreted following the National Committee for Clinical Laboratory Standards (NCCLS) recommendations. Nine drug/bug combinations were analyzed. The susceptibility methods utilized in each one of the MC were also evaluated. A total agreement between the results was obtained in nearly 76% of the drug/bug combinations. Very major and major errors were observed in 15.5% and 4.9% of the cases, respectively. The highest disagreements were observed for coagulase -negative staphylococci versus oxacillin (26.2% - very major error) and *Burkholderia cepacia* isolates versus imipenem (22.2% - very major error). The susceptibility method with the highest agreement rate was broth microdilution (94.0%) > Etest (92.8%) > agar dillution (92.4%). External quality assurance data obtained by surveillance programs such as SENTRY Antimicrobial Surveillance Program are not only helpful for detecting the emergence of patterns of antimicrobial resistance, but also for monitoring the performance of the participating microbiology laboratories.

Introduction

In the last years, the world has been challenged with the emergence of antimicrobial resistance. An increased number of species such as *Acinetobacter baumannii* and *Pseudomonas aeruginosa* has become resistant to all available antimicrobial agents. The clinical microbiology laboratories are faced with the task of accurately detecting emerging antibiotic resistance among several important bacterial pathogens.

A variety of antimicrobial susceptibility methods or commercial systems are available to the clinical microbiology laboratories for testing. These methods must be reliable and precise because their results will guide the antimicrobial therapy, a crucial step for the clinical management of infected patients. The report of false-susceptible results can lead to the misuse of antimicrobial agents resulting in therapeutic failure. In addition, the report of false-resistant isolates could result in an unnecessary administration of more expensive or more toxic antimicrobial agents.

The objective of this study was to compare the susceptibility testing results performed by the SENTRY monitoring laboratory with those of reported by the Latin American participating medical centers to assess the accuracy of data submitted.

Materials and Methods

Study design: Ten Latin American laboratories have participated of the SENTRY Antimicrobial Surveillance Program. Data collected from January 1997 to December 1999 was evaluated. Among the Latin American laboratories, 7 serve tertiary hospitals; 2 serve secondary hospitals, and 1 serves primary hospitals. The laboratories were distributed throughout nine cities in six countries: Sao Paulo, Rio de Janeiro and Florianopolis - Brazil; Buenos Aires and San Isidro - Argentina; Santiago (two centers) - Chile; Medellin - Colombia; Mexico City - Mexico; and Montevideo - Uruguay. In 1998, the center located in Montevideo was replaced by a Venezuelan center located in Caracas. Bacterial isolates were consecutively collected from hospitalized patient according to the site of infection: 1) Blood stream infections (BSI); 2) Low respiratory tract infection (LRTI); 3) Wound and soft tissue infections (WSTI); and 4) Urinary tract infections (UTI). Each isolate enclosed with its clinical and epidemiological data were sent to the coordinating laboratory at the University of Iowa College of Medicine (Iowa City, Iowa, USA). Just one isolate per patient was included in the study.

Organism identification: All pathogens were identified at the participating center using local routine methods and were confirmed at the coordinating laboratory using conventional methods or automated systems (Vitek and API, BioMerieux, St. Louis, MO, USA).

Susceptibility testing: Antimicrobial susceptibility tests were performed and interpreted at the coordinating laboratory using broth microdilution methods as described by the National Committee for Clinical Laboratory Standards (NCCLS M7 – A5). Antimicrobial agents were obtained from respective manufactures.

Quality control: Quality control was performed utilizing strains of the American Type Culture Collection: *S. aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, *E. coli* ATCC 25922, and *P. aeruginosa* ATCC 27853.

Categorical agreement: Broth microdilution performed at the coordinating laboratory was considered the reference method (gold standard). Broth microdilution results were compared to the antimicrobial susceptibility results submitted by the participating medical laboratories using the local routine tests (disk-diffusion; agar-dilution; broth microdilution ; MicroScan; Vitek; Pasco; Etest). Categorical agreement was considered when the test result was the same susceptibility category. Errors were determined by previous published methods: Very major error = false susceptible results divided by the number of true resistant strains; Major error = false-resistant results divided by the number of true susceptible strains. Rates of category agreement > 90.0%, very major < 1.5% and major error < 5.0% were considered acceptable. Key organism-drug combination from all sites were studied: *Staphylococcus aureus* – oxacillin , Coagulase-negative staphylococci – oxacillin, *Klebsiella* spp. / *E. coli* – broad-spectrum cephalosporins (ceftriaxone and ceftazidime), *Acinetobacter* spp. – imipenem, *Burkholderia cepacia*. – imipenem, and *Pseudomonas aeruginosa* – imipenem. SPSS for Windows Release 10.0.5 Standard Version was used to perform statistical analyses.

RESULTS

TABLE 1. Comparison between antimicrobial susceptibility results performed by the monitoring laboratory with those of reported by the Latin American medical centers - SENTRY Antimicrobial Surveillance Program 1997 to 1999.

Microrganism	Antimicrobial Agent	Number Tested	% Category Agreement	% Error (n)	
				Very Major	Major
S. aureus	oxacillin	1721	94.7	8.5 (49)	3.5(40)
CoNS[c]	oxacillin	777	76.7	26.2 (158)	11.5 (20)
***Klebsiella* spp.**	ceftriaxone	193	76.7	16.7 (7)	9.4 (12)
	ceftazidime	778	86.3	5.3 (11)	10.4 (56)
Escherichia coli	ceftriaxone	366	93.9	0.1 (1)	2.3 (8)
	ceftazidime	1317	94.3	15.7 (8)	3.1 (39)
***Acinetobacter* spp.**	imipenem	438	91.5	11.1 (5)	4.9 (19)
P. aeruginosa	imipenem	980	86.0	14.7 (26)	4.3 (32)
B. cepacia	imipenem	46	50.0	22.2 (4)	31.6 (6)
Total		**6616**	**76.4**	**15.5 (269)**	**4.9 (232)**

a – False-susceptible strains divided by the number of true resistant strains;
b – False-resistant strains divided by the number of true susceptible strains;
c – Coagulase - negative staphylococci.

TABLE 2. Performance of the antimicrobial susceptibility methods used by the Latin American medical centers[c] - SENTRY Antimicrobial Surveillance Program 1997 to 1999.

Methods	Number Tested (%)	% Category Agreement	% Error (n°)	
			Very Major[a]	Major[b]
Broth microdilution	150 (6.6)	94.0	33.3 (13)	1.8 (2)
Agar dilution	249 (10.9)	92.4	5.9 (5)	7.1 (10)
Vitek	607 (26.7)	91.9	7.7 (15)	10.2 (20)
MicroScan	156 (6.8)	88.4	12.1 (4)	6.6 (8)
Disk-diffusion	1037 (45.5)	86.5	14.4 (45)	5.8 (40)
Total	**2276[c]**	**88.4**	**12.4 (85)**	**6.2 (82)**

a – False-susceptible results divided by the number of true resistant results.
b – False-resistant results divided by the number of true susceptible results.
c – The antimicrobial susceptibility method was discriminated by the medical center for only 2,276 isolates.

Conclusions

- In general, low rates of category agreement (76.4%) and high rates of very major (15.5%) and major (4.9%) errors were observed in this study. These rates could be overestimated since only problematic drug/bug combinations were selected.
- Acceptable categorical agreement (>90.0%) was obtained only for *E. coli* versus broad-spectrum cephalosporins (94%) and *Acinetobacter* spp. versus imipenem (91.5%).

Conclusions (continued)

- Unacceptable categorical agreement (<90.0%) was observed for the following drug-bug combinations: CoNS versus oxacillin (76.7%), *Klebsiella* spp. versus broad-spectrum cephalosporins (76.7% - 86.3%), *P. aeruginosa* versus imipenem (86.0%) and *B. cepacia* versus imipenem (50.0%).
- The participating laboratories failed to detect oxacillin resistance in *S. aureus* and Coagulase-negative staphylococci isolates. CoNS versus oxacillin had the highest very major error rate (26.2%). This result might indicate that the participating centers are not adopting the latest NCCLS breakpoints for oxacillin or not complying with the NCCLS recommendations for detection of oxacillin-resistance. *S. aureus* versus oxacillin showed 8.5% of very major errors.
- High false susceptibility rates were encountered among *Klebsiella* spp. strains versus ceftriaxone (16.7%) and ceftazidime (5.3%). The discrepancies observed within this genus could be due to the high prevalence of broad-spectrum beta-lactamases (ESBL) producing *K. pneumoniae* strains in Latin America. Such strains could present differences in the susceptibility results due to the variation of the amount of enzyme produced.
- *Acinetobacter* spp. and *P. aeruginosa* are highly prevalent pathogens in Latin America. Curiously, high false-susceptibility rates were observed: 11.1% and 14.7%, respectively. The imipenem instability could be one of the reasons for false-resistant (major error) results. However, among these species, the major errors were within the acceptable rates (< 5.0%).
- High very major error rates observed among the *B. cepacia* strains (22.2%), could be due to the lack of standardized susceptibility testing methods for this species.
- Data obtained from the available demographic information showed that disk-diffusion was the most common antimicrobial susceptibility method used by the participating medical centers (45.5%) followed by the automated system Vitek (26.7%) > agar dilution method (10.9%) > MicroScan system (6.8%) > broth microdilution method (6.6%).
- The rank order of category agreement of antimicrobial susceptibility method/systems performed by the medical centers was broth microdilution (94.0%) > agar dilution (92.4%) > Vitek (91.9%) > MicroScan (88.4%) > disk-diffusion (86.5%).
- Unacceptable very major error rates varied from 5.9 % to 33.3% depending on the methodology utilized and species tested. 29 of 45 very major errors observed with the disk-diffusion methodology were detected with the combination CONS- oxacillin. When broth microdilution was used by the medical center, most of the very major errors (10/13) occurred within the combinations *Acinetobacter*-imipenem (7) and *P. aeruginosa* -imipenem (3). With the Vitek system, the most common error arose with the combination *P. aeruginosa* -imipenem (8). The errors occurred at similar rates in the diverse participating medical centers.
- External quality assurance data obtained by surveillance programs such as SENTRY Antimicrobial Surveillance Program are not only helpful for detecting the emergence of patterns of antimicrobial resistance, but also for monitoring the performance of the participating microbiology laboratories.

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