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Comparison of Three Automated Systems for Antimicrobial Susceptibility Testing of Gram-Negative Bacilli

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Several instruments for automated or semiautomated antimicrobial susceptibility testing are currently available. Three of these instruments, Autobac (General Diagnostics, Warner-Lambert Co., Morris Plains, N.J.), MS-2 (Abbott Laboratories, Dallas, Tex.), and AutoMicrobic system (AMS) (Vitek, Inc., Hazelwood, Mo.) were compared for antimicrobial susceptibility testing of gram-negative bacilli. A total of 207 isolates representing 29 species of gram-negative bacilli were tested simultaneously by each instrument and by a standardized disk diffusion reference method. Nine antimicrobial agents, including ampicillin, carbenicillin, cephalothin, gentamicin, tobramycin, amikacin, tetracycline, trimethoprim-sulfamethoxazole, and nitrofurantoin were tested. Discrepancies between the results of the automated and reference disk diffusion methods were resolved by agar dilution testing. Overall, 93% of the Autobac and MS-2 results and 83% of the AMS results were in agreement with the results obtained by the reference methods. The results of the Autobac, MS-2, and AMS systems respectively included 3.3, 2.3, and 4.2% major and very major discrepancies. Excessive testing discrepancies were found for certain drugs, including ampicillin, tetracycline, and nitrofurantoin, and for certain organisms, including species of *Providencia*, *Serratia*, and *Citrobacter*. The results of this comparison of three automated systems for antimicrobial susceptibility testing indicate that the Autobac and MS-2 instruments provided highly reliable results. The AMS needs further development of its susceptibility testing capability to eliminate an unacceptably high number of minor discrepancies.

Three automated systems are currently available for testing the susceptibility of gram-negative bacteria to antimicrobial agents. The Autobac system (General Diagnostics, Warner-Lambert Co., Morris Plains, N.J.) has been available for several years and has been found to produce susceptibility testing results comparable to those of disk diffusion (5) and microdilution methods (3). More recently, susceptibility testing capabilities have become available for the Abbott MS-2 instrument (Abbott Laboratories, Dallas, Tex.) and for the Vitek AutoMicrobic system (AMS) (Vitek, Inc., Hazelwood, Mo.). Published reports indicate that the MS-2 system gives results that agree 91 to 98% with those of reference methods (1, 4). Preliminary reports on the AMS have indicated that it gives results that agree 83 to 90% with those of reference methods (L. Smull, E. Mirro, and J. S. Nosanchuk, Abstr. Annu. Meet. Am. Soc. Microbiol. 1981, C123, p. 283; J. C. Paris, K. R. Cundy, C. Dietz, and W. Wong, Abstr. Annu. Meet. Am. Soc. Microbiol. 1981, C186, p. 293; H. Nadler, C. Dolan, L. Mele, H. George, M. Maduri, and D. Goldmann, Abstr. Annu. Meet. Am. Soc. Microbiol. 1981, C197, p. 295). This communication describes a simultaneous comparison of the three systems to assess the relative performance of each in testing the same group of gram-negative bacteria. The results demonstrate that agreement between Autobac and MS-2 results and those of reference methods was 93%, and agreement between AMS results and those of reference methods was 83%.

MATERIALS AND METHODS

Organisms. A total of 207 isolates, including 29 species of gram-negative bacilli, were tested by the three automated systems and by the reference methods. This collection of organisms included 142 fresh clinical isolates and 65 stock cultures of clinical isolates. Both common and unusual organisms were included (Table 1). Fresh clinical isolates were tested sequentially until the quota for each species was reached (Table 1). Stock cultures of recent clinical isolates were used to supplement the collection with unusual organisms.

Instruments. The Autobac MTS is a semiautomated instrument for susceptibility testing that monitors bacterial growth by making light scattering measurements. Autobac cuvettes were filled with standardized

TABLE 1. Organisms tested for antimicrobial susceptibility by three automated systems and disk diffusion

Organism	No. Tested	
	Fresh	Stock
Escherichia coli	29	0
Klebsiella pneumoniae	27	0
Pseudomonas aeruginosa	22	1
Proteus mirabilis	21	0
Serratia marcescens	17	2
Salmonella enteritidis	3	8
Shigella sp.	2	6
Enterobacter cloacae	6	1
Providencia stuarti	0	7
Citrobacter diversus	1	6
Enterobacter aerogenes	6	0
Morganella morganii	0	6
Citrobacter freundii	1	4
Acinetobacter calcoaceticus	0	5
Providencia alcalifaciens	0	4
Klebsiella oxytoca	1	2
Proteus rettgeri	2	1
Aeromonas hydrophila	0	3
Pseudomonas maltophilia	1	1
Salmonella typhi	0	2
Enterobacter agglomerans	0	1
Edwardsiella tarda	0	1
Klebsiella ozaenae	0	1
Proteus vulgaris	0	1
Vibrio vulnificus	0	1
Vibrio alginolyticus	0	1
Hafnia alvei	1	0
Pseudomonas fluorescens	1	0
Vibrio cholerae	1	0

suspensions of the organisms to be tested, elution disks were dropped into the cuvettes, and instrument readings were taken according to the manufacturer's instructions. The AMS is an automated instrument that employs a plastic card with microwells containing dried antibiotics (General Susceptibility Card) for susceptibility testing. Standardized suspensions of organisms were loaded into the cards in the filling chamber, and the cards were placed in the reader-incubator module for monitoring. All functions performed with the AMS were done according to the manufacturer's instructions. The MS-2 instrument employs disk elution methodology; a plastic cuvette, similar to that of the Autobac system, is used. Bacterial growth is monitored photometrically with light-emitting diodes. After the introduction of standardized suspensions of organisms into the cuvettes, testing was performed according to the manufacturer's instructions.

Experimental protocol. Organisms were tested simultaneously by the three automated systems and by disk diffusion (2) for susceptibility to ampicillin, carbenicillin, cephalothin, gentamicin, tobramycin, amikacin, tetracycline, trimethoprim-sulfamethoxazole, and nitrofurantoin. When the disk diffusion result was questionable (lack of agreement between the results of disk diffusion and those of two or three of the automated methods), agar dilution testing (6) was performed as a referee method. Discrepancies between the results of

TABLE 2. Antimicrobial susceptibilities of test strains as determined by disk diffusion, agar dilution, or both

Organism	No. of strains	Susceptibility[a]									
		Ampicillin	Carbenicillin	Cephalothin	Gentamicin	Tobramycin	Amikacin	Tetracycline	Trimethoprim-sulfamethoxazole	Nitrofurantoin
Escherichia coli	29	69,0,31	69,0,31	79,10,11	100,0,0	100,0,0	100,0,0	83,0,17	97,0,3	100,0,0
Klebsiella pneumoniae	27	4,0,96	7,0,93	74,4,22	78,4,18	78,4,18	100,0,0	26,26,48	74,0,26	41,15,44
Pseudomonas aeruginosa	23	0,0,100	100,0,0	0,0,100	78,17,5	91,0,9	91,4,5	0,0,100	0,0,100	0,0,100
Proteus mirabilis	21	95,0,5	100,0,0	95,0,5	100,0,0	100,0,0	100,0,0	0,5,95	100,0,0	0,0,100
Serratia marcescens	19	0,0,100	95,0,5	0,0,100	95,0,5	95,0,5	100,0,0	0,11,89	89,5,6	0,0,100
Salmonella enteritidis	11	91,0,9	91,0,9	91,0,9	100,0,0	100,0,0	100,0,0	91,9,0	91,0,9	100,0,0
Shigella spp.	8	50,0,50	50,0,50	75,0,25	100,0,0	100,0,0	100,0,0	75,0,25	100,0,0	100,0,0
Enterobacter spp.	14	7,7,86	71,0,29	21,8,71	93,0,7	93,0,7	100,0,0	50,14,36	93,0,7	64,0,36
Citrobacter spp.	12	17,8,75	42,0,58	58,17,25	100,0,0	100,0,0	100,0,0	92,0,8	83,8,9	100,0,0
Providencia spp.	14	64,0,36	100,0,0	14,29,57	50,29,21	64,7,29	93,7,0	7,7,86	71,7,12	0,36,64
Other	29	21,7,72	72,0,28	31,0,69	86,7,7	93,0,7	97,3,0	86,0,14	100,0,0	55,14,31

[a] Results are expressed percent susceptible, intermediate, and resistant, respectively for each drug.

TABLE 3. Performance of Autobac, AMS, and MS-2 in testing the susceptibilities of gram-negative bacilli

Method	No. of discrepancies (%)[a]		
	Very major	Major	Minor
Autobac	23 (1.2)	39 (2.1)	74 (4.0)
AMS	58 (3.1)	21 (1.1)	229 (12.4)
MS-2	31 (1.7)	11 (0.6)	92 (5.0)

[a] Total number of susceptibility tests performed by each system, 1,855.

automated and reference methods were recorded as follows: very major (resistant by reference method, susceptible by automated method), major (susceptible by reference method, resistant by automated method), minor (intermediate by reference method, susceptible or resistant by automated method; or susceptible or resistant by reference method, intermediate by automated method).

RESULTS

A total of 7,420 individual susceptibility tests were analyzed, and agar dilution testing was performed for 210 organism-antimicrobial agent combinations that had questionable disk diffusion results. The results for each automated method were compared to those of disk diffusion or agar dilution. When both disk diffusion and agar dilution results were available, the agar dilution result was used for analysis. Table 2 presents the antimicrobial susceptibilities of the 207 gram-negative bacteria included in the study. The organisms demonstrated expected patterns of susceptibility and resistance to the drugs tested. Table 3 summarizes the comparative susceptibility testing results for the three automated systems. Including all three categories of discrepancies, 7.3% of the Autobac results, 7.3% of the MS-2 results, and 16.6% of the AMS results failed to agree with the results of the reference methods. The Autobac system results included 1.2% very major discrepancies, 2.1% major discrepancies, and 4% minor discrepancies. The respective figures for the AMS system were 3.1, 1.1, and 12.4%, and those for the MS-2 system were 1.7, 0.6, and 5.0%. The numbers of combined major and very major discrepancies out of the total number of discrepancies were as follows: Autobac system, 62 (46%) of 136; AMS, 79 (26%) of 308; and MS-2, 42 (31%) of 134.

Of the nine drugs tested with each system, ampicillin, cephalothin, and nitrofurantoin were responsible for 49% of the discrepancies in the Autobac results (Table 4); ampicillin, tetracycline, and nitrofurantoin were responsible for 61% of the discrepancies in the AMS results; and tetracycline and nitrofurantoin were responsible for 51% of the discrepancies in the MS-2 results. Other drugs, such as aminoglycosides and trimethoprim-sulfamethoxazole, were responsible for very few discrepancies between the results of automated methods and those of reference methods.

Of the 29 bacterial species tested, several were associated with an excessive number of discrepancies (Table 5). *Providencia* species comprised 6% of the organisms tested but respectively accounted for 23, 12, and 16% of the discrepancies encountered in the Autobac, AMS and MS-2 results. *Serratia marcescens* comprised 9% of the organisms tested but accounted for 25% of the discrepancies in the AMS results,

TABLE 4. Distribution of susceptibility testing discrepancies by antimicrobial agent

Method	Discrepancies (% of total results) with:								
	Ampicillin	Carbenicillin	Cephalothin	Amikacin	Gentamicin	Tobramycin	Tetracycline	Trimethoprim-sulfamethoxazole	Nitrofurantoin
Autobac	21	11	13	7	9	4	10	8	15
AMS	19	12	7	4	4	7	18	6	24
MS-2	13	3	13	5	8	3	16	3	35

TABLE 5. Distribution of susceptibility testing discrepancies by organism

Method	Discrepancies (% of total results) with:							
	Klebsiella spp. (13%)[a]	*Serratia marcescens* (9%)	*Proteus* spp. (10%)	*Pseudomonas* spp. (11%)	*Escherichia coli* (14%)	*Providencia* spp. (6%)	*Citrobacter* spp. (5%)	Other (32%)
Autobac	15	5	8	4	4	23	13	28
AMS	13	25	15	10	3	12	2	20
MS-2	17	12	12	4	4	16	8	27

[a] Percentage in parentheses indicate how much of the total bacterial population tested was composed of the indicated organism(s).

and *Citrobacter* species comprised 5% of the organisms but accounted for 13% of the discrepancies in the Autobac results. Other organisms, such as *Escherichia coli* and *Pseudomonas aeruginosa*, were associated with a high correlation between automated and reference method results.

DISCUSSION

These studies demonstrate that the Autobac and MS-2 systems performed with nearly identical accuracy in a simultaneous comparison of antimicrobial susceptibility testing of gram-negative bacilli. The results of both instruments agreed 93% with the results of the reference methods, and these results agree with previously published findings (1, 3–5). The MS-2 and Autobac system results included only 2 and 3% combined major and very major discrepancies, respectively. The MS-2 system offers a high degree of automation, and although the system is limited to testing 9 or 10 antimicrobial agents per cuvette, the drugs to be tested can be selected by the user. Operation of the Autobac instrument requires greater technical involvement than is required by the other instruments analyzed, but 12 antimicrobial agents can be tested per cuvette, and the drugs to be tested can be selected by the user.

The AMS results agreed 83% with those of the reference methods, and this level of performance is substantially lower than that of the Autobac and MS-2 instruments. However, the AMS results included only 4% combined very major and major discrepancies, and most of the errors encountered with the AMS involved minor discrepancies and drugs used mainly for the treatment of urinary tract infections. Therefore, except for these relatively minor errors, the AMS also performed well, and we expect that with further refinement, the AMS will perform at an overall acceptable level. The AMS offers the advantage of a high degree of automation, and 13 antimicrobial agents are included for testing in each General Susceptibility Card.

In summary, the results of this simultaneous comparison of three automated instruments for antimicrobial susceptibility testing of gram-negative bacilli demonstrate that the Autobac and MS-2 instrument results provide acceptable agreement with the results of reference methods. The AMS results included an unacceptably high number of minor discrepancies, and this system should be further developed before it is accepted for routine use. All of the instruments provide results rapidly (3 to 5 h), and when coupled with rapid organism identification, they offer the potential for early result reporting. The instruments are also automated, which should improve the efficiency of antimicrobial susceptibility testing. These findings indicate that automated antimicrobial susceptibility testing can provide reliable results, improve efficiency, and provide more rapid reporting of results for improved patient care.

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