1635

An Evaluation of MicroScan WalkAway Results for Broad-Spectrum Beta-Lactams When Testing *Pseudomonas aeruginosa* (PSA)

S LERNER, L STEED, J BOSSO, RN JONES
Wayne State University, Detroit, MI, USA;
Medical University of South Carolina, Charleston, SC, USA;
JMI Laboratories, North Liberty, IA, USA

ECCMID 2007
JMI Laboratories
North Liberty, IA, USA
www.jmilabs.com
319.665.3370,
fax 319.665.3371
ronald-jones@jmilabs.com

ABSTRACT

Objectives: To compare contemporary clinical (CL) and challenge (CH) strains of PSA susceptibility (S) test results from an automated system (MicroScan WalkAway; 2 laboratories) against 6 broad-spectrum beta-lactams to results of reference broth microdilution (BMD) and consensus results from 3 validated methods (BMD, Etest, disk diffusion [DD]). Previous reports have documented high minor (mE; 10-32%) and very major (VME; false-S; 19%) errors among anti-PSA beta-lactams.

Methods: Each center tested CH (15) strains of PSA that included equally represented S and resistant (R) MICs across a wide range for tested agents (aztreonam [AZM], cefepime [FEP], ceftazidime [CAZ], imipenem [IPM], piperacillin [PIP], piperacillin/tazobactam [P/T]). 15 CL strains were also tested by MicroScan WalkAway (panel no. NEGMIC30 or NC32 and software no. LabPro 2.01) and 3 reference methods (BMD, Etest, DD). Categorical results from MicroScan WalkAway were compared to CLSI BMD results (see Table) as well as the consensus of all tests. Error limits for acceptability were those listed in the M23-A2 guideline.

Results: The table shows the comparisons of categorical agreement and the listed error rates occurred equally between participant sites and organism populations (CH, CL). Markedly elevated rates of mE were observed for AZM (21.7-23.3%), FEP (45.0-48.3%) and CAZ (20.0-23.3%), regardless of reference result selected for comparative analysis. More serious errors by MicroScan WalkAway of false-R (major error; ME) were also noted for the same agents, but false-S (VME) was detected (5.0-15.0%) for PIP and P/T. For drugs showing unacceptable mE or serious interpretive errors (ME), a systematic bias toward false-R MicroScan WalkAway results was found for AZM (10.0%), FEP (48.3%) and CAZ (16.7%). The skewing toward R was most extreme for FEP (3-fold greater than CAZ). PIP and P/T results trended toward false-S (VME) at a level of 10.0-11.7%.

Table. Error rates for the MicroScan WalkAway system when testing 30 PSA isolates in two laboratories.[a]

Antimicrobial agent (no. tested)	Percentage of errors by type: Compared to BMD result[b] Very major	Major	Minor	Compared to consensus result[b] Very Major	Major	Minor
Aztreonam (60)	0.0	3.3	21.7	0.0	3.3	23.3
Cefepime (60)	0.0	3.3	48.3	0.0	3.3	45.0
Ceftazidime (60)	1.7	6.7	23.3	0.0	6.7	20.0
Imipenem (60)	0.0	1.7	11.7	1.7	1.7	10.0
Piperacillin (60)	10.0	3.3	NA	15.0	3.3	NA
Piperacillin/tazobactam (60)	5.0	1.7	NA	10.0	0.0	NA

a. Results from University of South Carolina (Charleston, SC) and Wayne State University, Detroit Medical Center (Detroit, MI).
b. BMD = reference broth microdilution MIC results. Consensus result was determined from the reference BMD, disk diffusion and Etest values. Unacceptable levels of error are underlined. NA = not applicable.

Conclusions: These results corroborate findings of others that some automated susceptibility testing systems perform poorly when testing beta-lactam agents against PSA. Error rates documented in our medical centers for MicroScan WalkAway, using diverse PSA collections clearly indicates false-S and -R trends that seriously compromise patient care as well as misdirecting empiric treatment choices and formulary decisions. We recommend that our colleagues employ alternative methods such as BMD or agar diffusion tests (DD, Etest) to more accurately assess antimicrobial S among PSA.

INTRODUCTION

We read with great interest the evaluations of several commercial automated susceptibility testing systems by Sader et al. [1]. A component of those results compared the MicroScan WalkAway to a comprehensive list of five reference tests including the broth microdilution, agar dilution and disk diffusion methods described by the Clinical and Laboratory Standards Institute (CLSI; formerly the National Committee for Clinical Laboratory Standards [NCCLS]) , and detected unacceptable levels of minor (range, 10-32%) and very major (false-susceptible results; range 0-19%) errors among five tested broad-spectrum ß-lactam agents [1]. That study focused on a collection of geographically diverse *Pseudomonas aeruginosa* (100 strains) because the accuracy of automated systems has been challenged in recent and remote publications [6, 7]. We report here a two-center collaborative evaluation of the MicroScan WalkAway results for testing 60 *P. aeruginosa* strains compared to a CLSI reference test [2] and alternative methods validated in earlier studies by Burns and colleagues [5, 8].

MATERIALS AND METHODS

Each medical center tested a common challenge set (15 strains) of *P. aeruginosa* kindly provided by H.S. Sader [1] that included strains equally representing susceptible and resistant populations of MIC values across a wide range for the tested agents (aztreonam, cefepime, ceftazidime, imipenem, piperacillin, and piperacillin/tazobactam). Another 15 strains of local contemporary clinical strains were also tested by the MicroScan WalkAway (panel no. NEGMIC30 or NC32 and software no. LabPro 2.01) and three reference methods (frozen-form broth microdilution [TREK Diagnostics, Cleveland, OH], Etest [AB BIODISK, Solna, Sweden] and disk diffusion) [2, 4, 5].

Categorical results from the MicroScan WalkAway instrument were directly compared to those produced by the CLSI M7-A7 broth microdilution test [2] as well as the consensus of all other tests performed. Error limits for acceptability were those listed by the NCCLS [3] and earlier publications (J.H. Jorgensen, S.A. Crawford, M.K. Mansell, M.L. McElmeel, and L.C. Fulcher, Abstr. 106th ASM General Meeting, abstr. C-118, 2006) [1].

RESULTS

- Table 1 shows the comparisons of categorical agreement for all 60 results for each antimicrobial agent. Errors occurred near equally between the participant centers and between the two organism populations (challenge and clinical strains). Markedly elevated rates of minor errors were observed for aztreonam (21.7-23.3%), cefepime (45.0-48.3%) and ceftazidime (20.0-23.3%), regardless of the reference result (broth microdilution or consensus of three methods) selected for comparative analysis.

- More serious errors by MicroScan WalkAway system of false resistance were also noted for the same agents, and false-susceptible results were detected at rates of 5.0 to 15.0% for piperacillin with or without tazobactam.

- Among the antimicrobials showing unacceptable levels of minor or serious interpretive errors, a systemic bias toward false-resistant MicroScan WalkAway results was detected for aztreonam (10.0%), cefepime (48.3%) and ceftazidime (16.7%); see Tables 2 and 3. The skewing toward resistance is particularly severe for cefepime (three-fold greater than ceftazidime; Table 3).

- In contrast, the piperacillin and piperacillin/tazobactam results by the MicroScan WalkAway trended toward false susceptibility at a significant level of 10.0 to 11.7% (Table 2).

Table 1. Error rates for the MicroScan WalkAway system when testing 30 *P. aeruginosa* isolates in two different clinical laboratories.[a]

Antimicrobial agent (no. tested)	Percentage of errors by type: Compared to BMD result[b] Very major	Major	Minor	Compared to consensus result[b] Very Major	Major	Minor
Aztreonam (60)	0.0	3.3[c]	21.7[c]	0.0	3.3[c]	23.3[c]
Cefepime (60)	0.0	3.3[c]	48.3[c]	0.0	3.3[c]	45.0[c]
Ceftazidime (60)	1.7[c]	6.7[c]	23.3[c]	0.0	6.7[c]	20.0[c]
Imipenem (60)	0.0	1.7	11.7[c]	1.7[c]	1.7	10.0
Piperacillin (60)	10.0[c]	3.3[c]	NA[d]	15.0[c]	3.3[c]	NA[d]
Piperacillin/tazobactam (60)	5.0[c]	1.7	NA[d]	10.0[c]	0.0	NA[d]

a. Results from University of South Carolina (Charleston, SC) and Wayne State University, Detroit Medical Center (Detroit, MI).
b. BMD = reference broth microdilution MIC results [2, 4]. Consensus result was determined from the reference BMD, disk diffusion and Etest values.
c. Unacceptable levels of error.
d. NA = not applicable because of the lack of an intermediate category [4].

Table 2. Direction of automated system error (trends toward false susceptibility or resistance) when compared to the consensus categorical result.

Antimicrobial agent (no. errors)	MicroScan WalkAway category/ consensus category (no. occurrences)[a] More susceptible	More resistant
Aztreonam (16)	S/I (3), I/R (2)	R/S (2), I/S (2), R/I (7)[b]
Cefepime (29)	-	R/S (2), I/S (14), R/I (13)[b]
Ceftazidime (16)	S/I (2), I/R (1)	R/S (4), I/S (8), R/I (1)[b]
Imipenem (8)	S/R (1), S/I (2), I/R (2)	R/S (1), R/I (1), I/S (1)
Piperacillin (11)	S/R (9)[c]	R/S (2)
Piperacillin/tazobactam (6)	S/R (6)[c]	-

a. S = susceptible, I = intermediate and R = resistant categories.
b. Trend toward false resistance (≥10% of tests).
c. Trend toward false susceptibility (≥10% of tests).

Table 3. Example of a systematic trend toward resistance as observed for the MicroScan WalkAway when testing *P. aeruginosa* strains against cefepime (60 results from two medical centers[a]).

Consensus category (MIC, mg/L)	MicroScan WalkAway category: Susceptible (≤8)	Intermediate (16)	Resistant (≥32)
Susceptible (≤8)	19	14	2
Intermediate (16)	0	3	13
Resistant (≥32)	0	0	9

a. Results recorded at Wayne State University Detroit Medical Center (Detroit, MI) and Medical University of South Carolina (Charleston, SC).

CONCLUSIONS

- These results corroborate the findings of others (J.H. Jorgensen et al., Abstr. 106th ASM General Meeting, abstr. C-118, 2006) [1, 6, 7] that some automated susceptibility testing systems perform poorly when testing ß-lactam agents against *P. aeruginosa*.

- Error rates documented in our two medical centers for MicroScan WalkAway using fresh clinical isolates and a challenge pseudomonal collection clearly indicates both false-susceptible and -resistant trends that could misdirect empiric therapy choices and formulary decisions.

- We urge the manufacturer to re-evaluate their product for five of the six tested broad-spectrum ß-lactams; and additionally, we recommend that our clinical laboratory colleagues employ alternative methods such as agar diffusion tests (disk diffusion and/or Etest) to more accurately assess the antimicrobial susceptibilities of *P. aeruginosa* isolates [7, 8].

ACKNOWLEDGEMENTS

The co-authors wish to thank the following individuals for technical and organizational contributions or in the provision of the challenge strains: H.S. Sader, D.J. Biedenbach, T. Painter and N. O'Mara-Morrissey. The study was funded by a collaborative educational/research grant from JMI Laboratories (North Liberty, IA) and Elan Pharmaceuticals (San Diego, CA).

SELECTED REFERENCES

1. Sader HS, Fritsche TR, Jones RN. Accuracy of three automated systems (MicroScan WalkAway, VITEK, and VITEK 2) for susceptibility testing of *Pseudomonas aeruginosa* against five broad-spectrum ß-lactam agents. *J Clin Microbiol*. 2006; 44: 1101-4.
2. Clinical and Laboratory Standards Institute. (2006). *M7-A7, Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard - seventh edition.* Wayne, PA: CLSI.
3. National Committee for Clinical Laboratory Standards. (2001). *Approved guideline M23-A2: Development of in vitro susceptibility testing criteria and quality controls parameters, 2nd ed.* Wayne, PA: NCCLS.
4. Clinical and Laboratory Standards Institute. (2006). *M100-S16, Performance standards for antimicrobial susceptibility testing; sixteenth informational supplement.* Wayne, PA: CLSI.
5. Clinical and Laboratory Standards Institute. (2006). M2-A9. *Performance standards for antimicrobial disk susceptibility tests; approved standard - ninth edition.* Wayne, PA: CLSI.
6. Biedenbach DJ, Marshall SA, Jones RN. Accuracy of cefepime antimicrobial susceptibility testing results for *Pseudomonas aeruginosa* tested on the MicroScan WalkAway System. *Diagn Microbiol Infect Dis*. 1999; 33: 305-7.
7. Burns JL, Saiman L, Whittier S, Krzewinski J, Liu Z, Larone D, et al. Comparison of two commercial systems (Vitek and MicroScan-WalkAway) for antimicrobial susceptibility testing of *Pseudomonas aeruginosa* isolates from cystic fibrosis patients. *Diagn Microbiol Infect Dis*. 2001; 39: 257-60.
8. Burns JL, Saiman L, Whittier S, Larone D, Krzewinski J, Liu Z, et al. Comparison of agar diffusion methodologies for antimicrobial susceptibility testing of *Pseudomonas aeruginosa* isolates from cystic fibrosis patients. *J Clin Microbiol*. 2000; 38: 1818-22.