Two Rapid Phenotypic Antimicrobial Susceptibility Tests (AST) for Gram Negative Bacteremia (GNB)

Cassiana E. Bittencourt MD[1] , Brenda Herrera MT [1], Hiroki Saito MD, MPH[2], Sara Sirajuddin MD[2], Wint Thu Hun MD[2], Steven Park, MD, PhD[2], PhD, Ellena Peterson, PhD[1], Lauri Thrupp, MD, FIDSA, FSHEA[2]

[1]Department of Pathology and Laboratory Medicine, University of California Irvine, School of Medicine, [2]Department of Medicine, University of California Irvine, School of Medicine, Irvine, CA

UC, Irvine
714-456-5439
bittencc@uci.edu

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Background

Clinical outcomes of GNB are optimized with rapid AST and real time Antibiotic Stewardship (AS). To facilitate prompt AS we use a rapid direct disc diffusion test (RDDDT), which had been validated against CLSI standard disk diffusion (DD) and Vitek-2.[1-2] Phenotypic AST is the gold standard because molecular assays may not detect all phenotypic resistance. Here we compared results from the RDDDT to another phenotypic based AST test, the Accelerate Pheno system, AXDX (Accelerate Diagnostics, Tucson, AZ) which is an automated approach for rapid ID (<2h) and AST (7h) from positive blood cultures (BC).

Objectives

- To compare the AST results from the RDDDT and AXDX to a standard of care (SOC), consisting of Vitek-2 and standard DD
- To compare AXDX to RDDDT for antibiotic susceptibility results reportable rate and timing of antibiotic stewardship Team actionable reporting to RDDDT

Study Design & Methods

- Prospective Observational Study
- Duration from April to June 2018
- Samples were tested in parallel by AXDX, RDDDT and SOC
- For RDDDT
  - Positive BC were inoculated directly without inoculum adjustment onto Mueller-Hinton plates, using swabs as in CLSI standard DD and antibiotic discs were added
  - Plates were read twice a day, ~ 9 am or 3pm, after at least 9 hours incubation. Results were interpreted in accordance with CLSI criteria
- Results of the AXDX and RDDDT were compared to SOC and assessed as:
  - Complete agreement (CA), Minor (MI) discrepancies (S ←→I or I←→ R), Major (M) discrepancies (R→ S), and Very major (VM) discrepancies (S→R)
- We compared the AST reportability, and timing of AS Team actionable reporting between AXDX and RDDDT

Results

Figure 1. Pathogens

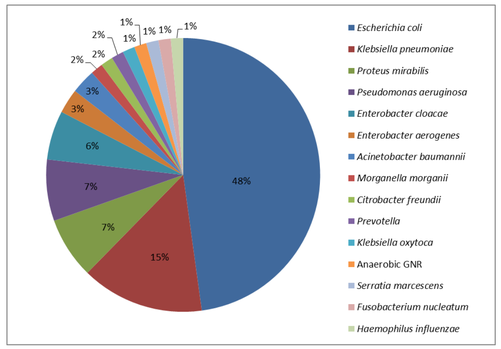

Figure 3. Time to result

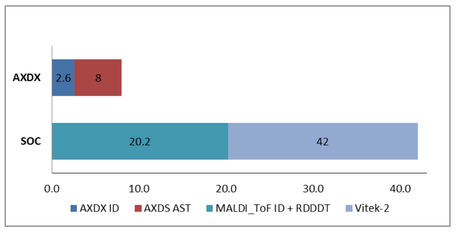

Figure 2 A: AXDX reportability

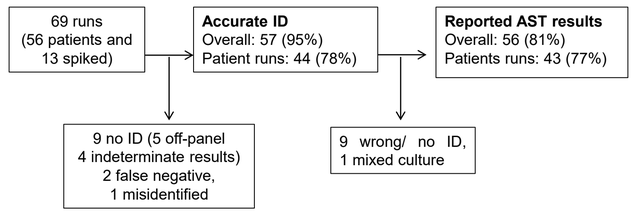

Figure 2 B: RDDDT reportability

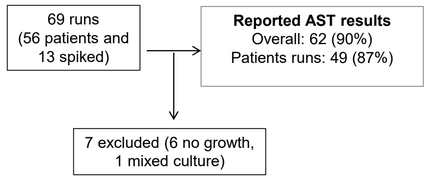

Table 1. Timing of reporting and delay to AS intervention

	Time of reporting		Delay to actionable reporting	
AST report Time	AXDX	RDDDT	AXDX	RDDDT
8AM-5PM*	17 (40%)	49 (100%)	17 (8h)	49 (20h)
5PM-12AM	18 (42%)	-	18 (15h)	-
12AM-8AM	8 (18%)	-	8 (15h)	-
No AST reported	13 (23%)	7 (12%)	13 (42h)	7 (42h)
Overall predicted mean delay			19h	22.7h

* Active antibiotic stewardship timeframe

Table 2. AST performance *versus* SOC

	N		CA		VM		M		MI		Susceptible		Resistant	
Antibiotic	**AXDX**	**RDDDT**	**AXDX**	**RDDDT**	**AXDX**	**RDDDT**	**AXDX**	**RDDDT**	**AXDX**	**RDDDT**	**AXDX**	**RDDDT**	**AXDX**	**RDDDT**
Amikacin	54	-	54 (100%)	-	0	-	0 (0%)	-	0 (0%)	-	52 (96%)	-	2 (4%)	-
Ampicillin-Sulbactam	42	-	34 (81%)	-	1 (6%)	-	0 (0%)	-	7 (17%)	-	21 (50%)	-	16 (38%)	-
Aztreonam	48	54	48 (100%)	52 (96%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (3.7%)	33 (69%)	39 (72%)	15 (31%)	15 (28%)
Cefazolin	31	48	18 (58%)	35 (73%)	0 (0%)	0 (0%)	0 (0%)	1 (11%)	13 (42%)	12 (25%)	4 (13%)	9 (19%)	14 (45%)	25 (52%)
Cefepime	54	62	48 (89%)	51 (82%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	6 (11%)	10 (16%)	40 (74%)	47 (76%)	10 (19%)	11 (18%)
Ceftazidime	54	61	48 (89%)	59 (97%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	6 (11%)	1 (1.6%)	36 (67%)	42 (69%)	17 (31%)	18 (29%)
Ceftriaxone	50	57	49 (98%)	53 (93%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (7%)	31 (62%)	35 (61%)	19 (38%)	21 (37%)
Ciprofloxacin	54	62	52 (96%)	60 (97%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (4%)	2 (3%)	31 (57%)	34 (55%)	22 (41%)	27 (43%)
Ertapenem	50	57	47 (94%)	50 (88%)	0 (0%)	0 (0%)	0 (0%)	2 (4%)	3 (6%)	5 (9%)	42 (84%)	48 (84%)	8 (16%)	8 (14%)
Gentamicin	54	-	53 (98%)	-	0 (0%)	-	0 (0%)	-	1 (2%)	-	39 (72%)	-	14 (26%)	-
Meropenem	49	59	48 (98%)	53 (90%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	6 (10%)	43 (88%)	50 (85%)	4 (8%)	5 (8%)
Piperacillin-Tazobactam	55	62	51 (93%)	53 (85%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (7%)	8 (13%)	44 (80%)	50 (81%)	11 (20%)	12 (19%)
Tobramycin	54	62	49 (91%)	57 (92%)	0 (0%)	1 (10%)	0 (0%)	0 (0%)	5 (9%)	5 (8%)	37 (69%)	44 (71%)	10 (19%)	10 (16%)
Trimethoprim-Sulfamethoxazole	-	56	-	51 (91%)	-	1 (3.4%)	-	1 (3.7%)	-	3 (5%)	-	27 (48%)	-	29 (52%)
All	**649**	**640**	**599 (92%)**	**574 (90%)**	**2 (1%)**	**2 (1.1%)**	**0 (0%)**	**6 (1.5%)**	**48 (7%)**	**58 (9%)**	**453 (70%)**	**425 (66%)**	**162 (25%)**	**181 (28%)**

Abbreviations: CA: Categorical Agreement, VM: Very Major discrepancies; M: Major discrepancies; MI: Minor discrepancies

Discussion and Conclusion

- AXDX is a useful tool for rapid ID, and phenotypic AST
- The categorical AST agreement was comparable for the inexpensive RDDDT (90%) versus AXDX (92%)
- AST results averaged 12 h and 34 h sooner than RDDDT (read twice daily) and Vitek-2, respectively
- AXDX AST's were reportable in only 77% of patients; of these results only 40% would be reported during our AS Team intervention period. From published data, the clinical benefit from rapid methods have been shown to be dependent on real time AS interventions,[3-6] especially for de-escalation
- If all the AST results are taken into consideration, the overall predicted average delay to actionable reporting between the two methods was comparable, 19 h for AXDX vs 23 h for the RDDDT
- Our findings highlight the need for extended AS Team intervention in order to maximize the impact of results from any rapid AST method

Limitations

- Small prospective pilot study to evaluate AXDX *versus* RDDDT performance in a single center
- AXDX was not reported to EMR and chart review was not performed for all patients to assess clinical intervention and antibiotic optimization. However, review of all extended-spectrum beta-lactamases (ESBL) and carbapenem resistant Enterobacteriaceae (CRE) showed 5/12 (42%) cases warranted escalation

References

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4. 2. Tristan T. Timbrook et al. The Effect of Molecular Rapid Diagnostic Testing on Clinical Outcomes in Bloodstream Infections: A Systematic Review and Meta-analysis. Clin Infect Dis 64:15–23. 2017
5. Tamar F. Barlam et al. Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Clin Infect Dis 62:10. 2016.
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