Direct antimicrobial susceptibility testing for acute urinary tract infection – comparison of AI-assisted zone interpretation and conventional susceptibility testing methods

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INTRODUCTION

Direct antimicrobial susceptibility testing (dAST) from urine samples using disc diffusion methods is in widespread use in some countries, allowing for the provision of results earlier than traditional AST methods, at a lower cost. However, it is a labour-intensive technique subject to reader variability and its use remains controversial, largely because there is no published method or standardized breakpoints.

This study examines the veracity of disc dAST from urine samples containing clinically significant Enterobacterales and investigates the use of the artificial intelligence (AI) plate interpretation capability of the APAS® Independence (Clever Culture Systems, Switzerland) with APAS®-AMR module in providing a solution in lieu of manual plate-in-hand reading or minimum inhibitory concentration methodology using Vitek 2 (BioMérieux).

METHODOLOGY

192 urines from patients with suspected uncomplicated UTI were enrolled in this study. Mueller Hinton E plates (Edwards Group, 04091) were inoculated using a sterile cotton swab dipped into the urine sample and a RETRO C80 inoculator. A panel of 12 antimicrobial discs was applied. The plates were incubated according to CLSI guidelines and subsequently read by APAS (dAST-APAS), and plate-in-hand methods using digital calipers (d-AST manual). Significant isolates were tested in the Vitek 2, providing an MIC and S/R interpretation, and by disc diffusion by APAS Independence (iAST-APAS) and plate-in-hand method (iAST-manual) using the same disc panel used for dAST. The Vitek 2 result was used as the reference result for comparison against the test methods. Results were examined and documented in a blinded form and categorical agreement (CA – No errors), Minor Errors (MiE), Major errors (ME), and very major errors (VME) were determined (Table 1). Analysis of the difference in mm between automated and manual reads were also performed (Table 2). Performance of Vitek versus iAST-manual, i.e., a baseline comparison of two established methods, was additionally scrutinised.

RESULTS

- From the 82 significant isolates availed (Table 3), over 1800 unique disc reads resulted. Table 4 displays both raw and adjusted agreement and error levels.
- When comparing iAST-manual v Vitek, of note is the VME of 1.6%. In our opinion this is the expected intrinsic rate of error of the system differences between disc and MIC testing as part of this study.
- From the total of 1840 unique disc reads, 89% of automated versus manual reads were within 3mm, with >80% within 2 mm (Table 2).
- Errors between S/I/R determination for Vitek and CLSI methods for isolate testing (iAST-manual v Vitek) were apparent, indicating some intrinsic variability in methods (Fig. 3) where both manual and APAS measurement indicated a "S" result, but the Vitek was "R" with a high MIC value.
- In one example (Fig. 4), both plate-in-hand and APAS assessment indicated an "S" and Vitek "R" for KZ30. In this case the Vitek result is correct due to the presence of mutants close to the edge of the zone and mutants within AMC30. The isolate was identified as containing an ESBL.

Table 1. Classification of errors

		Reference		
		S	I	R
Test	S	No Error	Minor Error	Very Major Error
	I	Minor Error	No Error	Minor Error
	R	Major Error	Minor Error	No Error

Table 2. Differences between APAS and manual reads

	Difference between APAS and manual reads (mm)					
	0 to 1	1 to 2	2 to 3	3 to 4	>=4	Total reads
Isolates	595	196	55	28	18	892
	67%	22%	6%	3%	2%	
Direct sensitivity	531	197	69	50	101	948
	56%	21%	7%	5%	11%	
Overall	1126	393	124	78	119	1840
	61%	21%	7%	4%	6%	

Table 3. Organisms represented in this study

Organism name	No. of isolates
Escherichia coli	64 (including 6 ESBL)
Klebsiella pneumoniae	8
Enterobacter aerogenes	3
Proteus mirabilis	2
Citrobacter freundii	2
Citrobacter koseri	1
Enterobacter cloacae	1
Proteus vulgaris	1

Table 4. Performance of APAS v Manual v Vitek

	dAST-APAS v dAST-Manual	iAST-APAS v iAST-manual	dAST-manual v Vitek	dAST-APAS v Vitek	iAST-manual v Vitek
CA – raw measurements	95.4% (904/948)	97.2% (867/892)	93.1% (824/885)	91.3% (842/922)	93.7% (866/924)
CA – expert rules modified			93.8% (820/874)	92.3% (838/908)	94.6% (861/910)
MiE– raw measurements	2.6% (25/948)	2.8% (25/892)	4.6% (41/885)	4.3% (40/922)	4.0% (37/924)
MiE– expert rules modified			4.2% (37/874)	3.9% (35/908)	3.4% (31/910)
ME raw measurements	0.9% (9/948)	0% (0/892)	0.7% (6/885)	1.1% (10/922)	0.6% (6/924)
ME – expert rules modified			0.7% (6/874)	0.9% (8/908)	0.7% (6/910)
VME– raw measurements	1.1% (10/948)	0% (0/892)	1.6% (14/885)	3.3% (30/922)	1.6% (15/924)
VME – expert rules modified			1.3% (11/874)	2.8% (25/908)	1.3% (12/910)

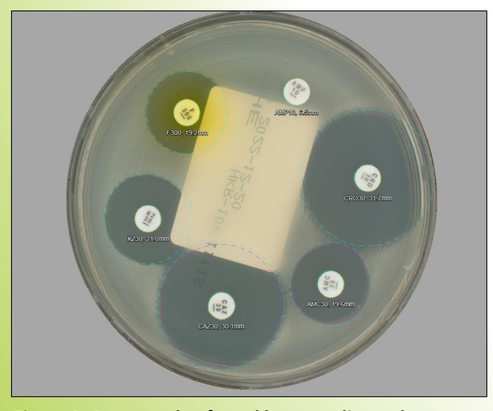

Figure 1. An example of good lawn quality and accurate APAS measurements

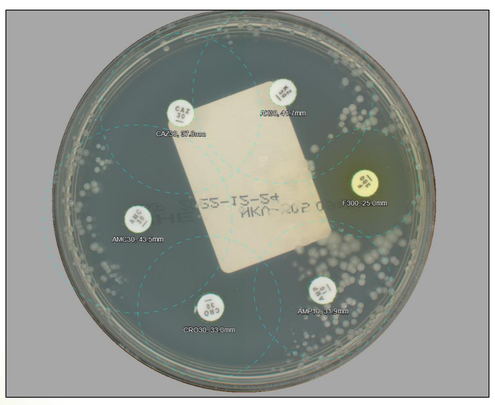

Figure 2. Low lawn quality from dAST leading to errors in measurement.

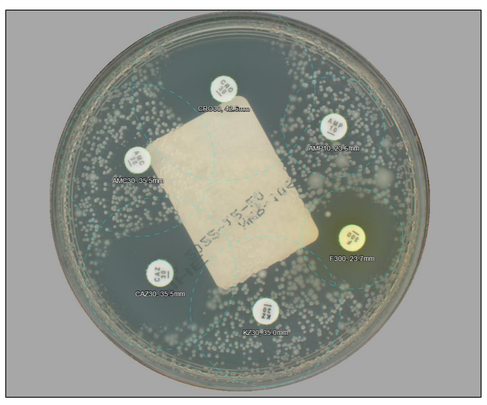

Figure 3. Example of a discrepant analysis resulting in a VME (*E. coli* and AMC30 disc).
iAST-manual = 19mm (S), iAST-APAS = 18.5 (S), Vitek = R (MIC = 16).

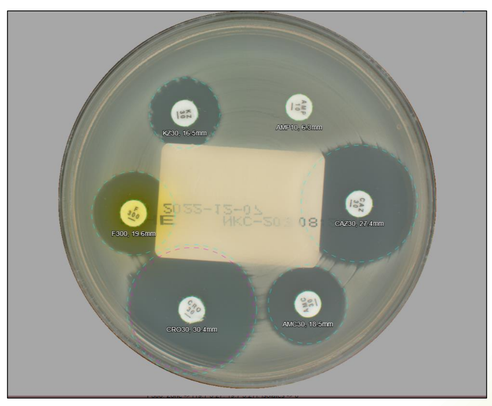

Figure 4. Example of a discrepant analysis resulting in a VME (K. aerogenes (ESBL) and KZ30 disc). dAST-manual = 16mm (S), dAST-APAS = 17.0 (S), Vitek = R (MIC ≥64).

CONCLUSIONS

- There is no significant difference in the manual measurements of zone sizes compared to APAS measurements for the determination of categorical agreement (dAST-APAS v dAST-Manual, iAST-APAS and iAST-manual), with very low error rates demonstrated.
- It is apparent that low inoculum levels on dAST plates (with both APAS and manual interpretation) contribute significantly to VMEs (Fig.1, Fig.2). APAS is able to flag low inoculum levels for review, therefore mitigating these VMEs, further improving performance by reducing the actual VME rate.
- Additional discrepant analysis is likely to further improve the already high performance of APAS, where integration of expert rules, lawn quality checks, and isolate detection checks will mitigate a large proportion of errors not captured in this raw analysis.
- The performance of disc sensitivity testing directly from uncomplicated UTI samples is comparable to testing isolated organisms in the Vitek system, and offers clear turn-around time improvements. This approach is being considered for gram-negative urinary isolates where clear sensitivity patterns are present, and would be limited to selected frontline urinary antimicrobials. This is expected to deliver cost and time benefits for the laboratory.

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