Resistance mechanisms and automated methods

It is well-known that automated methods, due to their use of small inocula have difficulties in detecting heteroresistant populations, leading to false susceptible results and consequently very major errors. Also well-known is the difficulties of automated methods in testing beta-lactam antimicrobials and detection of beta-lactamases.

We have screened papers and presentations during 2005 to 2009, including only well recognised authors and magazines, such as Clinical Microbiology & Infection, J. Clinical Microbiology, J. Medical Microbiology, Int. J. Antimicrobial Agents and presentations at the ICAAC and ECCMID.

MicroScan

Jones et al (1) report from CAP: false automated system results for VRSA, VISA and piperacillin/tazobactam with P. aeruginosa. Suboptimal MRSA and ESBL detection in commercial automated systems.

Sader et al (2) report an unacceptable rate (21 – 32 %) of Very Major errors for piperacillin/tazobactam with P. aeruginosa.

Unda et al (4) report false resistance to amikacin with the MicroScan WalkAway 96 system as well as major errors with gentamicin and tobramycin; concluding that the system was not reliable for susceptibility testing of P. aeruginosa to amikacin.

Sader et al (7) studied the accuracy of MicroScan, Vitek and Vitek 2 for susceptibility testing of P. aeruginosa to 5 broad spectrum beta-lactams. All systems tested exhibited a high, unacceptable level of very major (false susceptible) errors for piperacillin/tazobactam (19-27%) and minor error rates were elevated for cefepime and aztreonam (8-32%), leading to consistent trends towards false resistance.

Jones et al (9) detected errors by automated systems in CAP surveys. Numerous false susceptible and false resistant were noted for each antimicrobial. False positive ESBL results for a CMY-2 AmpC producing strain. Besides, false susceptibility to linezolid and false resistance to cefepime (2005), false susceptibility to amox+clav and piperacillin/tazobactam (2006).

Juretschko et al (10) reported unacceptable levels of errors (minor, major and very major) with false susceptibility to piperacillin-tazobactam and piperacillin and false resistance to aztreonam, cefepime and ceftazidime in P. aeruginosa.

Kulah et al (11) studied imipenem resistance in A. baumannii and MicroScan showed the worst performance with 25 % very major errors and 44.6 % minor errors.

Juretschko et al (15) found that 25 % of all cystic fibrosis isolates identified as MSSA by automated methods were mecA positive and therefore MRSA (false susceptibility, very major error).

Gordon et al (20) describe the failure of MicroScan to detect heteroresistance to carbapenems in a patient with E. aerogenes bacteremia and conclude: reliance on automated susceptibility testing, while is more rapid than disc diffusion methods, may result in a delay in detecting or inability to detect the development of resistance.

Phoenix

Juretschko et al (10) reported false resistance to aztreonam and cefepime for P. aeruginosa Kehl et al (12) found that the Phoenix automated system made false positive identification of vancomycin resistant enterococci(VRE).

Arslan U et al (14) studied automated systems to detect HLR to gentamicin in enterococci. 4 of 5 isolates with gentamicin MICs 256 ug/ml, were found susceptible by Phoenix. Strains with aac-aph gene were reported false susceptible .

Juretschko et al (15) found that 25 % of all cystic fibrosis isolates identified as MSSA by Phoenix were mecA positive and therefore MRSA (very major error).

Boyd et al (16) report misidentification of K. pneumoniae carbapenemase (KPC) as ESBL by the Phoenix instrument and conclude that KPC can remain undetected or misinterpreted as ESBL by automated systems. Routine phenotypic testing should be performed.
Boyd et al (18) mention the erroneous reporting of ESBL producers by Phoenix and Vitek 2.
9 of 22 non-ESBL were reported as ESBL by Phoenix (specificity 59 %). The authors conclude that false positive ESBL may be reported by Phoenix and that implementation of phenotypic testing should be considered in ESBL "positive" isolates by automated methods.

Fisher et al (19) compared Phoenix with disc diffusion for identification of ESBL, AmpC and KPC producers. The Phoenix system misclassified nearly 50% of the isolates as ESBL positive. Besides a high false positive detection rate for AmpC. Of 8 KPC producing isolates the Phoenix system reported 50% as meropenem and imipenem susceptible (very major error). The authors conclude that we need reliable methods to detect these important resistance mechanisms in the clinical laboratory.

Vitek 2

Jones et al (1) report from CAP 30 % false susceptibility with piperacillin/tazobactam and P. aeruginosa.

Sader et al (2) report an unacceptable rate (21-32%) of Very major errors for piperacillin/tazobactam with P. aeruginosa.

Ceyssens et al (3) report that VITEK-2 overestimates the number of ESBLs among Enterobacteriaceae, that may lead to unnecessary use of carbapenems.

Karatuna et al (5) studied the reliability of carbapenem resistance in P. aeruginosa, by automated systems (Vitek2) and concluded that laboratories using automated systems should consider using at least a second method to validate intermediate or resistant results for carbapenems tested against Pseudomonas spp.

Tokatlidou D et al (6) observed the over detection of imipenem resistance by Vitek 2 in VIM 12 producing K. pneumoniae with Etest low level carbapenem MICs.

Sader et al (7) found an unacceptable level of very major (false susceptible) errors for piperacillin/tazobactam (19-27 %) as well elevated minor error rates for cefepime and aztreonam, when testing against P. aeruginosa.

Navon-Venezia et al (8) found that when testing cefepime susceptibility of ESBL producing E. coli and K. pneumoniae the Vitek 2 results, were major errors. The high proportion errors and major errors negate the use of Vitek 2 for cefepime MIC determination when ESBL positive strains are considered.

Jones et al (9) studied errors of automated methods according to CAP surveys. False susceptibility to imipenem when testing a SME-1 producing S. marcescens. Besides false susceptibility to meropenem and false resistance to cefoxitin (2003). False susceptibility to piper/tazo, amikacin imipenem and piperacillin (2004). False susceptibility to linezolid (2005). False resistance to cefoxitin (2006).
Juretschko et al (10) reported unacceptable levels of error with false susceptibility to piperacillin/tazobactam and imipenem and false resistance to aztreonam, cefepime and ceftazidime.

Pitout et al (13) report that Vitek Legacy and Vitek 2 failed to detect piperacillin/tazobactam resistance in 74 % of 101 pipera/tazo resistant, ESBL producing strains, especially CTX-M-15 producing isolates that co-produced OXA-1.

Arslan et al (14) found that Vitek 2 failed to detect HLR gentamicin resistance in E. faecium isolates with aac-aph gene (false susceptible, very major error).

Juretschko et al (15) conclude that the VITEK 2 misidentified 25 % of MRSA isolated from cystic fibrosis patients as MSSA (very major error).

Boyd et al (16) report misidentification of K. pneumoniae carbapenemases (KPC) as ESBL by the Vitek 2 and conclude that KPC isolates can evade detection with automated methods and be misinterpreted as ESBL.

Bulik et al (17) compared meropenem MICs for KPC producing K. pneumoniae by Etest, broth microdilution and Vitek2.When comparing Vitek2 MICs to broth microdilution, only 22 % of isolates were in agreement.

Boyd et al (18) indicates the erroneous reporting of ESBL producers by Vitek 2. 13 of 22 non-ESBLs were reported as ESBL positive by the Vitek2 (specificity 40.9%). Implementation of phenotypic testing should be considered.

References

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