Multi-site Evaluation Of Sensititre Susceptibility MIC EUCAST Standard Panel Using EUCAST Breakpoints For *Staphylococcus* Species

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Overview

Purpose: The manual read and automated read MIC results from the Thermo Scientific™ Sensititre™ susceptibility MIC EUCAST standard panel for staphylococci (EUSTAPF panel) containing ceftaroline, cefoxitin,clindamycin, daptomycin, fusidic acid, erythromycin, gentamicin, linezolid, levofloxacin, norfloxacin, moxifloxacin, mupirocin, rifampicin, teicoplanin, telavancin, tetracycline, tobramycin, trimethoprim/sulfamethoxazole and vancomycin were evaluated at three study sites.

Methods: Reproducibility and clinical isolate testing of the EUSTAPF panel were conducted according to ISO 20776-2:2007[1]. Testing was performed according to manufacturer's instructions. Results were compared to the broth microdilution reference method stated in ISO 20776-1:2006[2].

Results: The EUSTAPF panel proved to be an accurate alternative to the broth microdilution reference method for MIC determination of the antimicrobial agents tested for methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-susceptible *S. aureus* (MSSA) and coagulase negative staphylococcus (CNS).

Introduction

The Thermo Scientific™ Sensititre™ System consists of 96-well microtitre plates containing dilutions of antimicrobials dried in individual wells (available in both standard and custom formats) as well as instrumentation to enable inoculation and interpretation (see figure 1). The Sensititre System utilizes true MIC results rather than extrapolated (MIC) results and offers flexible, customizable testing options to accommodate formularies and laboratories of all sizes conducting antimicrobial susceptibility and identification (AST/ ID) testing.

Methods

Reproducibility

Reproducibility testing of 10 staphylococcal isolates in triplicate over 3 consecutive days was performed on the EUSTAPF panel at each study site. The EUSTAPF panel was inoculated and tested according to manufacturer's instructions; panels were read using the Thermo Scientific™ Sensititre™ Vizion™ system (manual read) and Thermo Scientific™ Sensititre™ ARIS™ system (automated read); results were interpreted using the Thermo Scientific™ Sensititre™ SWIN™ Software system.

Clinical isolate testing

Three hundred and one clinical isolates (including 74 MRSA, 77 MSSA and 150 CNS) were tested using the EUSTAPF panel; results were compared to the broth microdilution reference method. The EUSTAPF panel was inoculated and tested according to manufacturer's instructions; panels were read using both the Sensititre Vizion system (manual read) and Sensititre ARIS system (automated read); results were interpreted using the Sensititre SWIN Software system. Trimethoprim-sulfamethoxazole with CNS was only read using the manual read method (according to manufacturer's instructions).The broth microdilution reference method was performed according ISO 20776-1:2006.

FIGURE 1. Thermo Scientific SensititreSystem

Quality control

Recommended quality control (QC) organisms were tested daily. Purity checks and colony counts were performed daily on the broth microdilution reference method according to ISO 20776-1:2006. Purity checks were conducted daily on the EUSTAPF panel and colony counts performed periodically according to manufacturer's instructions.

Data Analysis

Using EUCAST breakpoints, essential agreement (EA), categorical agreement (CA) and discrepancy rates of the results obtained from the EUSTAPF panel were calculated according to ISO 20776-2:2007. The ISO 20776-2:2007 acceptance criteria are ≥90% EA, ≥90% CA and a very major discrepancy (VMD) and major discrepancy (MD) rate of ≤3%. Minor discrepancies (mD) were also reported.

Results

Reproducibility

Intra- (daily) and inter- (between days) reproducibility of staphylococcal isolates for both manual read and auto read was within ±1 dilution of the mode for all antimicrobials tested for ≥95% of results from all study sites. Where the mode could not be calculated, the median was used.

Clinical isolate testing

Essential agreement (EA)

Of the total 301 clinical isolates tested during the study, EA was >95% for all antimicrobials, for all organism groups for both manual read and auto read methods. Therefore EA of all antimicrobials was deemed acceptable according to ISO 20776-2:2007.

Categorical agreement (CA)

Of the total 301 clinical isolates tested during the study, CA was >95% for all antimicrobials, for all organism groups for both manual read and auto read methods with the exception of:

- tetracycline with CNS using manual read (94%)
- trimethoprim-sulfamethoxazole with CNS using manual read (93%)

Therefore CA of all antimicrobials was deemed acceptable according to ISO 20776-2:2007.

Discrepancy rates

There were exceptionally few VMD, MD and mD for all antimicrobials tested during the study. Where there were discrepancies, discrepancy rates were within acceptability criteria defined by ISO 20776-2:2007. There were no VMD or MD observed for tetracycline and trimethoprim-sulfamethoxazole at any of the 3 study sites; mD for these two antimicrobials were only observed on CNS.

Conclusion

The EUSTAPF panel proved to be an accurate alternative to the broth microdilution reference method for MIC determination of ceftaroline, cefoxitin,clindamycin, daptomycin, fusidic acid, erythromycin, gentamicin, linezolid, levofloxacin, norfloxacin, moxifloxacin, mupirocin, rifampicin, teicoplanin, telavancin, tetracycline, tobramycin, trimethoprim/sulfamethoxazole and vancomycin antimicrobial agents tested with MRSA, MSSA and CNS.

References

1.Clinical Laboratory Testing and in vitro Diagnostic Test Systems - Susceptibility Testing of Infectious Agents and Evaluation of Performance of AST Devices – Part 2:Evaluation of Performance of AST devices. ISO 20776-2:2007

2.Clinical Laboratory Testing and in vitro Diagnostic Test Systems - Susceptibility Testing of Infectious Agents and Evaluation of Performance of AST Devices – Part 1: Reference Method for Testing the in vitro Activity of antimicrobial Agents Against Rapidly Growing Aerobic Bacteria Involved in Infectious Diseases. ISO 20776-1: 2006.

LT2260 March 2016