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Clinical Evaluation of QMAC-dRAST for Direct and Rapid Antimicrobial Susceptibility Test with Gram-Positive Cocci from Positive Blood Culture Bottles

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Background: Timely intervention in the treatment of bloodstream infection is important for prescription of appropriate antimicrobials. With prompt determination of the antimicrobial susceptibility of a causative agent, rapid antimicrobial susceptibility test (AST) can help select the appropriate antimicrobial therapy. This clinical study is for evaluation of the clinical performance of the QMAC-dRAST for rapid AST directly from positive blood culture (PBC)s with Gram-positive cocci.
Methods: A total of 115 PBC samples with Gram-positive organisms (76 *Staphylococcus* spp. and 39 *Enterococcus* spp.) were evaluated by the QMAC-dRAST system, and their pure culture isolates were evaluated by the MicroScan WalkAway (Beckman Coulter, USA) as the comparative AST system. Thirteen antimicrobial agents were included, and the agreement and discrepancy rates of the QMAC-dRAST system (Quantamatrix Inc., Republic of Korea) compared to the MicroScan WalkAway were calculated. To resolve discrepancies, the broth microdilution method was performed.
Results: The QMAC-dRAST system exhibited a categorical agreement rate of 94.9% (1,126/1,187) and an essential agreement rate of 98.3% (1,167/1,187). The QMAC-dRAST system yielded very major (false-susceptible) errors at 1.0% (5/485), major (false-resistant) errors at 1.3% (9/693), and minor errors at 4.0% (47/1,187) compared to the MicroScan WalkAway. The QMAC-dRAST system significantly eliminated 30 hours of total turnaround time by combination of direct inoculation of PBC and an image-based approach.
Conclusion: The results of the QMAC-dRAST system were highly accurate. Thereby, the QMAC-dRAST may provide essential information to accelerate therapeutic decisions for earlier and adequate antibiotic treatment and patient management in clinical settings.
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Key Words: Antimicrobial drug resistance, Bacteremia, Bioengineering, Microbial sensitivity test

INTRODUCTION

Timely intervention in the treatment of bloodstream infection is of high significance to provide precise antimicrobial [1,2]. With prompt determination of antimicrobial susceptibility of causative agent, rapid AST can help selecting appropriate antimicrobial therapy. Furthermore, it is expected that rapid antimicrobial susceptibility test (AST) can contribute to the decrease of redundant laboratory tests, healthcare-associated expenses and prevention of empirical therapy [3-5]. In most of clinical settings, clinicians utilize phenotypic approaches for the antibiotic profiling of patients. Currently, most of clinical settings utilize phenotypic AST methods including manual methods such as broth microdilution method, disk diffusion method,

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E-test and commercially available automated systems based on turbidity measurement such as MicroScan WalkAway (Beckman Coulter, Brea, CA, USA), VITEK 2 (bioMerieux, Hazelwood, MO, USA) and PHOENIX (BD Bioscience, San Jose, CA, USA).

These conventional AST methods require relatively longer turnaround time (TAT) due to preceding preparation procedures including blood culture, Gram stain and overnight subculture onto solid medium of flagged positive culture samples [6]. For reducing TAT, various researchers have tried to directly process the positive blood culture (PBC) samples without subculture involving overnight culture [7]. AST methods utilizing direct inoculation from PBC had previously been reported with significant agreement rates compared to reference methods [8,9]. However, these previous studies reported that direct AST methods were insufficient to handle Gram-positive bacteria, mainly applicable for Gram-negative organisms [10-12]. The QMAC-dRAST (Quantamatrix Inc., Seoul, Republic of Korea) system has been introduced in the clinical microbiology laboratory for expedite treatment of bloodstream infection and antibiotic-resistant strain infections via a direct inoculation of PBC [13]. This system determines the antimicrobial susceptibility of bacteria within six hours without performing any additional separation processes and inoculum size measurement [13-15].

The objective of this study was to evaluate the accuracy of QMAC-dRAST AST system with faster protocol for staphylococci and enterococci cocci isolates originated from blood culture bottles. The accuracy was compared to that from MicroScan WalkAway plus system, commonly used as an automated AST system.

MATERIALS AND METHODS

1. Samples

The clinical evaluation of this study was conducted from June 2015 to June 2016 at Seoul National University Hospital (SNUH). For blood culture, BACTEC Plus Aerobic/F and Anaerobic/F culture bottles were used in BACTEC FX automated incubation system (Becton Dickinson Company, NJ, USA) and BacT/Alert FA Plus and SN bottles in a BacT/Alert 3D system (bioMerieux Inc., Marcy l'Étoile, France). PBC samples containing mono-bacterial infection with staphylococci and enterococci were included in the study. The PBC samples identified as Gram-negative rod, yeast and *Streptococcus* spp. were excluded from this study.

2. Quality control strains

Quality control testing of QMAC-dRAST panels was conducted when they were manufactured at the factory and delivered to the laboratory. For the quality control organisms, E. faecalis ATCC 29212 and S. aureus ATCC 29213 strains were used.

3. QMAC-dRAST system as the direct and rapid AST

A PBC sample was collected from the positive-flagged blood bottle with a 1 mL syringe and transferred to a sterile tube without any additional process. To achieve the optimum inoculation concentration for the QMAC-dRAST system, a 10 μL of the PBC sample was mixed with 4 mL of liquid-state 0.5% agarose at 37-40°C. Next, 10 μL of the mixture was inoculated in the 96-well format QMAC-dRAST Gram-positive (GP) panel containing 13 antimicrobials at various concentrations. Due to the capillary effect, the micro-patterned radial shape of the well helped the agarose mixture spread and form a disk shaped matrix in the entire well. After solidification of the agarose matrix at room temperature, 100 μL of culture medium was loaded into well of QMAC-dRAST GP panel to rehydrate the freeze-dried antimicrobial antibiotics. The culture medium with antibiotics was diffused into the agarose matrix. The QMAC-dRAST GP panel was incubated for 6 hours at a 35°C and images of each well were taken both at the time of inoculation (0 hour) and the experimental termination (after 6 hours). After acquisition and analysis of images from each well, the minimum inhibitory concentration (MIC) values and the interpretative determination were reported based on the interpretive criteria of the the Clinical & Laboratory Standards Institute (CLSI) [16].

4. MicroScan WalkAway plus system

For comparative data, MicroScan WalkAway plus system was processed in parallel with QMAC-dRAST system. A drop of PBC sample was inoculated onto blood agar plate. The inoculated blood agar plates were incubated at 35°C in 5% CO_2 to enable bacterial growth. After 20 hours incubation, the bacterial colonies were formed on the agar plate of a pure culture, as clinical isolates.

5. Broth microdilution (BMD) method as the confirmatory AST

The BMD method, recommended by CLSI, was used as a reference method to establish consensus categorical and MIC dis-

crepancies occurred between the QMAC-dRAST system and MicroScan WalkAway plus system for each organism-antimicrobial combination [16]. For the BMD method, the antibiotic solutions were prepared from the stock solution. The antimicrobial agents at the appropriate concentration, which was determined by CLSI recommendation, were loaded on the bottom of 96 microwell plates (SPL Life Sciences, Pocheon, Korea). After preparation of the BMD panel, 10 μL of clinical isolates at a final concentration of 5×10^5 CFU/mL was inoculated into well. The BMD tests were performed in triplicate. After 16-20 hours of incubation at 35°C, the MIC value of the BMD tests was determined as the concentration of the complete inhibition in growth as compared to the control. In case of results from erythromycin, linezolid, and tetracycline, MIC was determined in the lowest concentration where the trailing growth began [16]. For trimethoprim/sulfamethoxazole, MIC was the concentration in which there is ≥80% reduction in growth as compared to the control [16].

6. Identification of bacteria from PBC bottles

For the analysis of bacterial identification, a PBC sample was processed using the Sepsityper kit (Bruker Daltonics Inc., Billerica, MA, USA) prior to analysis using the Bruker MALDI-TOF Biotyper system (Bruker Daltonics Inc., Billerica, MA, USA) by trained staff at SNUH. In detail, 1.0 mL of sample from a PBC sample was transferred to a 1.5 mL centrifuge tube. A 200 μL aliquot of lysis buffer (provided) was added to the PBC sample, and the mixture was vortexed prior to centrifugation. Following centrifugation, the supernatant was removed, and the bacterial pellet was resuspended in 1.0 mL of wash buffer (provided), vortexed, and centrifuged. The supernatant was discarded, and the pellet was resuspended in 300 μL of deionized water. Then, 900 μL of 100% ethanol was added, and the mixture was vortexed and centrifuged at 13,000 rpm for 1 min. The ethanol was discarded, and the sample was again centrifuged. The pellet was allowed to dry completely. After drying, 70% formic acid (Sigma-Aldrich, St. Louis, MO, USA) at the same volume as the pellet (~10 μL) was added and mixed. The same volume (~10 μL) of acetonitrile (Sigma-aldrich, St. Louis, MO, USA) was added, and the pellet was resuspended. One microliter of the final supernatant was dropped onto the MALDI plate and dried. It was then overlaid with 1 μL of the α-Cyano-4-hydroxycinnamic acid (HCCA) matrix solution. After drying the sample, MALDI-TOF MS analysis was performed on a Bruker Microflex MALDI-TOF mass spectrometer and interpreted by MALDI Biotyper software (version 3.1).

7. Data analysis

The MIC values analyzed from the QMAC-dRAST system and BMD method were translated into clinical categories (susceptible, intermediate or resistant) according to the interpretative criteria of the CLSI based on bacterial identification results. The MIC values from MicroScan WalkAway plus were determined according to the manufacturer's instructions including the interpretation of results. The concordance in results from tests was recorded as agreement (Categorical agreement (CA), i.e., agreement of interpretive results between test method and the reference. Essential agreement (EA), i.e., agreement within plus or minus, one two-fold dilution of the new device under evaluation with the reference method) while susceptibility discrepancies were classified as very major errors (VME, i.e., sensitive with the test method but resistant with the reference method, false susceptible), major errors (ME, i.e., resistant with the automation method but susceptible with the reference method, false resistant), or minor errors (mE, i.e., susceptible or resistant versus intermediate).

RESULTS

1. Direct identification of PBCs with Gram-positive cocci for interpreting AST results

Bacterial identification of PBC samples of Gram-positive cocci was simultaneously performed by Sepsityper kit and MALDI Biotyper. Since it is possible to obtain identification results of PBC samples from Sepsityper kit and MALDI Biotyper within 2 hours, it was possible to interpret the MIC values at the termination of AST. Clinical samples identified with species level were only included for this study. The clinical samples identi-

Table 1. Distribution of Gram-positive cocci from PBCs used in this study

Genus	Species	No. (%)
Staphylococcus spp.	*Staphylococcus aureus*	42 (36.5)
	Staphylococcus epidermidis	23 (20.0)
	Staphylococcus haemolyticus	8 (7.0)
	Staphylococcus hominis	3 (2.6)
Enterococcus spp.	*Enterococcus faecium*	24 (20.9)
	Enterococcus faecalis	14 (12.2)
	Enterococcus gallinarum	1 (0.9)
Total		115 (100)

fied with genus level or were not identical with identification of MicroScan WalkAway plus system were also excluded from in this evaluation. Total 115 positive blood culture samples of Gram-positive cocci were investigated and a complete list of tested organisms was presented in Table 1. There were 76 *Staphylococcus* spp. including 42 *S. aureus*, 23 *S. epidermidis*, 8 *S. haemolyticus*, and 3 *S. hominis*. There were 39 *Enteoroccocus* spp. including 24 *E. faecium*, 14 *E. faecalis* and one *E. gallinarum*. These GPC isolates were used for interpreting MIC and interpretative AST results.

2. The performance of the QMAC-dRAST system

The AST results of the QMAC-dRAST system for Gram-positive cocci from 115 (1,187 antimicrobial agent-microorganism combinations) PBC samples are shown in the Table 2. For 115 Gram-positive samples, through the QMAC-dRAST system, we observed 94.9% of CA and 98.3% of EA between QMAC-RAST system and MicroScan WalkAway plus system, respectively. The discrepancy rates of QMAC-dRAST were VME of 1.0% (5/485), ME of 1.2% (9/693) and mE of 4.0% (47/1,187), respectively. The highest CA was observed from ampicillin (100%), followed by linezolid (99.1%). Lowest CA was shown from erythromycin (84.3%) and ciprofloxacin (89.6%). The QMAC-dRAST system yielded over 90% of CA for each antimicrobial except two antimicrobial agents; erythromycin and ciprofloxacin. The majority of discrepancies was classified as mEs.

The discrepancy rates for to QMAC-dRAST results compared to those from MicroScan WalkAway plus system in species level are shown in Table 3. The QMAC-dRAST system yielded CA 96.8%, EA 97.8% in *S. aureus*, CA 90.9%, EA 98.7% in CNS and CA 96.5, EA 98.7% in *Enterococcus* spp., respectively (Table 3).

Specifically, four VMEs and two MEs were observed from *S. aureus* in the QMAC-dRAST. Regarding the lowest CA from erythromycin-*S. aureus* combination, majority of discrepancies were determined as mEs. One of 18 oxacillin-resistant *S. aureus* and one of 15 erythromycin-resistant *S. aureus* were not determined as resistant by the QMAC-dRAST system. From majority of antimicrobial agents except erythromycin, CA exceeded 95% in *S. aureus*. For CNS, only one VME and seven MEs were observed in the QMAC-dRAST results. Among the seven MEs, three MEs were detected from trimethoprim/sulfamethoxazole and mEs occurred mostly from ciprofloxacin, gentamicin, erythromycin, and vancomycin. For *Enterococcus* spp., no VME and ME were found, however, mE were mostly observed from erythromycin and vancomycin. All vancomycin-resistant *Enterococcus* were detected as resistant by the QMAC-dRAST system. In overall, mE accounted for the most of errors from the tests with all antimicrobial agents (Table 3).

The QMAC-dRAST results were available within 6 hours after inoculation into the QMAC-dRAST GP panel, which were

Table 2. Agreement rates in AST results between the QMAC-dRAST and MicroScan WalkAway plus system for Gram-positive cocci

Antimicrobial agents	No. of test	No. (%) of error			CA (%)	EA (%)
		VME	ME	mE		
Ampicillin	39	0	0	0	100	100
Ciprofloxacin	115	0	1 (2.4)	11 (9.6)	89.6	99.1
Clindamycin	76	0	0	1 (1.3)	98.7	100
Erythromycin	115	1 (1.4)	2 (5.3)	15 (13.0)	84.3	88.7
Gentamicin	73	1 (3.4)	0	5 (6.8)	91.8	100
Levofloxacin	115	0	0	4 (3.5)	96.5	97.5
Linezolid	115	0	0	1 (0.9)	99.1	100
Oxacillin	42	1 (5.6)	0	0	97.6	100
Penicillin	115	2 (2.0)	0	0	98.3	97.4
Rifampin	76	0	2 (3.1)	0	97.4	98.7
Trimethoprim/Sulfamethoxazole	76	0	4 (6.3)	0	94.7	98.7
Tetracycline	115	0	0	4 (3.5)	96.5	100
Vancomycin	115	0	0	6 (5.2)	94.8	99.1
Total	1,187	5 (1.0)	9 (1.2)	47 (4.0)	94.9	98.3

Abbreviations: CA, category agreement; EA, essential agreement; VME, very major error; ME, major error; mE, minor error.
With the results obtained with the standard method as comparator. Errors between the results compared to the standard methods with MicroScan WalkAway plus system were resolved using BMD method (see text for details).

Table 3. Discrepancy rates and agreement rates of two AST systems in this clinical evaluation classified into combination of antimicrobial agents and bacterial species

Microorganism(s) and antimicrobial agents	No. of samples with susceptibility		No. (%) of errors			CA (%)	EA (%)
	S	R	VME	ME	mE		
S. aureus (n=42)							
Ciprofloxacin	29	13	0	0	2 (4.8)	95.2	100
Clindamycin	27	15	0	0	1 (2.4)	97.6	100
Erythromycin	27	15	1 (6.7)	1 (3.7)	6 (14.3)	81	83.3
Gentamicin	32	7	0	0	0	100	100
Levofloxacin	30	12	0	0	0	100	100
Linezolid	42	0	0	0	0	100	100
Oxacillin	24	18	1 (5.6)	0	0	97.6	92.9
Penicillin	1	41	2 (4.9)	0	0	95.2	92.9
Rifampin	41	1	0	0	0	100	100
Trimethoprim/Sulfamethoxazole	42	0	0	1 (2.4)	0	97.6	97.6
Tetracycline	35	7	0	0	1 (2.4)	97.6	100
Vancomycin	42	0	0	0	0	100	100
Total	372	129	4 (3.1)	2 (0.5)	10 (2.0)	96.8	97.8
CNS (n=34)							
Ciprofloxacin	8	26	0	1 (12.5)	7 (20.6)	76.5	97.1
Clindamycin	17	16	0	0	0	100	100
Erythromycin	9	25	0	1 (11.1)	4 (11.8)	85.3	91.2
Gentamicin	7	22	1 (4.5)	0	5 (15.2)	81.8	100
Levofloxacin	8	26	0	0	3 (8.8)	91.2	100
Linezolid	34	0	0	0	0	100	100
Penicillin	0	34	0	0	0	100	100
Rifampin	24	10	0	2 (8.3)	0	91.2	97.1
Trimethoprim/Sulfamethoxazole	21	13	0	3 (14.3)	0	91.2	100
Tetracycline	27	7	0	0	3 (8.8)	91.2	100
Vancomycin	34	0	0	0	4 (11.8)	88.2	100
Total	189	179	1 (0.6)	7 (3.7)	26 (7.0)	90.9	98.7
Enterococcus (n=39)							
Ampicillin	15	24	0	0	0	100	100
Ciprofloxacin	4	33	0	0	2 (5.1)	94.9	100
Erythromycin	4	34	0	0	5 (12.8)	87.2	92.3
Levofloxacin	6	33	0	0	1 (2.6)	97.4	100
Linezolid	39	0	0	0	1 (2.6)	97.4	100
Penicillin	14	25	0	0	0	100	100
Tetracycline	26	13	0	0	0	100	100
Vancomycin	24	15	0	0	2 (12.8)	94.9	97.4
Total	132	177	0	0	11 (4.5)	96.5	98.7

Abbreviations: S, susceptible; R, resistant; CA, category agreement; EA, essential agreement; VME, very major error; ME, major error; mE, minor error.

With the results obtained with the standard method as comparator. Discrepancies among results obtained from MicroScan WalkAway plus system were identified by the BMD method (see text for details).

The number of results within the intermediate category can be calculated by subtracting the resistant and susceptible results from the number of isolate-antibiotic combinations tested.

concordant with previous research [13].

DISCUSSION

Rapid and accurate antimicrobial prescription is essential for successful management of BSI patients. In general, antimicrobial

regimens are empirically chosen until AST results are available. Since empirical broad-spectrum antimicrobial treatment could induce the emergence of antimicrobial resistant microorganisms, it is important for clinicians to prescribe requisite antibiotics for reduction of mortality and morbidity. Faster identification of antimicrobial susceptibility can reduce TAT via expediting appropriate antimicrobial choices. Through expedite antibiotic profiling, patient management can be further improved by reducing numbers of redundant laboratory tests and procedures [5]. As the current AST systems necessitate longer TAT and manual procedures, there needs automated form of rapid AST system for both reducing TAT and redundant procedures [17].

However, the antimicrobial prescription process using current automated AST system takes more than two days from existence of causative agents in blood culture bottle, involving sequential experimental step; sub-culture to form the colony from the PBC samples and to perform conventional AST. To accelerate this process, many research groups have focused on the development of methodology by directly applying the PBCs into the current AST system.

One experimental approach has utilized inoculum directly from PBCs for AST, rather than cultured microbial colonies. Several studies have already compared this direct AST methods to the current methods used in the laboratory. These direct AST methods using inoculation from PBCs had quite acceptable results for Gram-negative rods, but not for Gram-positive cocci [8,9,11,12,18]. For higher accuracy of direct AST result for Gram-positive bacteria, many studies have attempted and chosen methods requiring multiple procedures, such as high speed centrifugation [5], reagent treatments [19], short incubation time on solid medium [20]. As a result, accuracy of direct AST results for Gram-positive cocci were quite acceptable with comparable agreement. However, these additional processes are not suitable for clinical application due to laborious works.

The other strategy is the application of novel techniques such as MALDI-TOF mass spectrometry, PCR-based techniques, microarrays, and microfluidics [7]. The QMAC-dRAST system detects the response of individual bacteria to antimicrobials by time-lapse microscopic observation and image analysis of micro-colony formation at the various concentrations of antimicrobial agents [13].

This study focused on whether the QMAC-dRAST system could be utilized routinely to reduce time for AST results of staphylococci and enterococci by comparing results between QMAC-dRAST system from PBCs and MicroScan WalkAway plus system.

As a result, the QMAC-dRAST system evaluated 1,187 antimicrobial Gram-positive cocci combinations, showing 94.9% overall CA and 98.3% overall EA, with only 1.0% VME and 1.3% ME. These results indicate that the antimicrobial agreement rate of QMAC-dRAST from PBC with Gram-positive cocci was comparable or superior to that of other studies [9,12,21]. It is noteworthy that the detection of oxacillin-resistant staphylococci with the QMAC-dRAST system was accurate even if one VME was observed in *S. aureus*, this result agreed with other standard AST reporting for oxacillin-resistance detection, for the agreement rates ranged from 95 to 100% [10,22]. Also, the QMAC-dRAST yielded high accuracy for the detection of vancomycin-resistant enterococci. Interestingly, no errors were observed for vancomycin and linezolid, the most frequently used antibiotics to treat systemic infections caused by staphylococci and enterococci. These results showed that QMAC-dRAST system can precisely detect the antimicrobial resistance of medically significant GPC.

However, there lie some limitations to this study. The QMAC-dRAST panel did not cover some concentrations of oxacillin necessary for interpreting CNS. The up-to-date version of panel fully cover concentrations for CNS. In addition, further studies are necessary to confirm the reliability of this method with various kinds of pathogens with different resistance phenotypes.

We hereby report the favorable performance of direct AST via the QMAC-dRAST system with PBC sample. It is expected that the QMAC-dRAST system may provide the essential information to accelerate therapeutic decisions in a timely manner by decreasing the time from flagged positive signal to obtain AST results for Gram-positive cocci. This could offer the possibility of having susceptibility test results available on the same day that a positive blood culture was detected.

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REFERENCES

1. Schefold JC, Hasper D, Volk HD, Reinke P. Sepsis: time has come to focus on the later stages. Med Hypotheses 2008;71:203-8.
2. Gherardi G, Angeletti S, Panitti M, Pompilio A, Di Bonaventura

G, Crea F, et al. Comparative evaluation of the Vitek-2 Compact and Phoenix systems for rapid identification and antibiotic susceptibility testing directly from blood cultures of Gram-negative and Gram-positive isolates. Diagn Microbiol Infect Dis 2012;72: 20-31.
3. Barenfanger J, Drake C, Kacich G. Clinical and financial benefits of rapid bacterial identification and antimicrobial susceptibility testing. J Clin Microbiol 1999;37:1415-8.
4. Munoz-Dávila MJ, Yagüe G, Albert M, García-Lucas T. Comparative evaluation of Vitek 2 identification and susceptibility testing of Gram-negative rods directly and isolated from BacT/ALERT-positive blood culture bottles. Eur J Clin Microbiol Infect Dis 2012;31:663-9.
5. Bazzi AM, Rabaan AA, Fawarah MM, Al-Tawfiq JA. Direct identification and susceptibility testing of positive blood cultures using high speed cold centrifugation and Vitek II system. J Infect Public Health 2017;10:299-307.
6. Jo SJ, Park KG, Han K, Park DJ, Park YJ. Direct identification and antimicrobial susceptibility testing of bacteria from positive blood culture bottles by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and the Vitek 2 system. Ann Lab Med 2016;36:117-23.
7. Pulido MR, García-Quintanilla M, Martín-Peña R, Cisneros JM, McConnell MJ. Progress on the development of rapid methods for antimicrobial susceptibility testing. J Antimicrob Chemother 2013; 68:2710-7.
8. Ling TK, Liu ZK, Cheng AF. Evaluation of the VITEK 2 system for rapid direct identification and susceptibility testing of gram-negative bacilli from positive blood cultures. J Clin Microbiol 2003;41:4705-7.
9. de Cueto M, Ceballos E, Martinez-Martinez L, Perea EJ, Pascual A. Use of positive blood cultures for direct identification and susceptibility testing with the Vitek 2 system. J Clin Microbiol 2004;42:3734-8.
10. Ligozzi M, Bernini C, Bonora MG, De Fatima M, Zuliani J, Fontana R. Evaluation of the VITEK 2 system for identification and antimicrobial susceptibility testing of medically relevant gram-positive cocci. J Clin Microbiol 2002;40:1681-6.
11. Funke G, Funke-Kissling P. Use of the BD PHOENIX Automated Microbiology System for direct identification and susceptibility testing of gram-negative rods from positive blood cultures in a three-phase trial. J Clin Microbiol 2004;42:1466-70.
12. Chen JR, Lee SY, Yang BH, Lu JJ. Rapid identification and susceptibility testing using the VITEK 2 system using culture fluids from positive BacT/ALERT blood cultures. J Microbiol Immunol Infect 2008;41:259-64.
13. Choi J, Jeong HY, Lee GY, Han S, Han S, Jin B, et al. Direct, rapid antimicrobial susceptibility test from positive blood cultures based on microscopic imaging analysis. Sci Rep 2017;7:1148.
14. Choi J, Jung YG, Kim J, Kim S, Jung Y, Na H, et al. Rapid antibiotic susceptibility testing by tracking single cell growth in a microfluidic agarose channel system. Lab Chip 2013;13:280-7.
15. Choi J, Yoo J, Lee M, Kim EG, Lee JS, Lee S, et al. A rapid antimicrobial susceptibility test based on single-cell morphological analysis. Sci Transl Med 2014;6:267ra174.
16. CLSI. Performance standards for antimicrobial susceptibility testing: Twenty-four informational supplement. CLSI document M100-S24. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.
17. Mittman SA, Huard RC, Della-Latta P, Whittier S. Comparison of BD Phoenix to Vitek 2, MicroScan MICroSTREP, and Etest for antimicrobial susceptibility testing of *Streptococcus pneumoniae*. J Clin Microbiol 2009;47:3557-61.
18. Hansen DS, Jensen AG, Nørskov-Lauritsen N, Skov R, Bruun B. Direct identification and susceptibility testing of enteric bacilli from positive blood cultures using VITEK (GNI+/GNS-GA). Clin Microbiol Infect 2002;8:38-44.
19. Lupetti A, Barnini S, Morici P, Ghelardi E, Nibbering PH, Campa M. Saponin promotes rapid identification and antimicrobial susceptibility profiling of Gram-positive and Gram-negative bacteria in blood cultures with the Vitek 2 system. Eur J Clin Microbiol Infect Dis 2013;32:493-502.
20. Idelevich EA, Schüle I, Grünastel B, Wüllenweber J, Peters G, Becker K. Acceleration of antimicrobial susceptibility testing of positive blood cultures by inoculation of Vitek 2 cards with briefly incubated solid medium cultures. J Clin Microbiol 2014;52: 4058-62.
21. Howard WJ, Buschelman BJ, Bale MJ, Pfaller MA, Koontz FP, Jones RN. Vitek GPS card susceptibility testing accuracy using direct inoculation from BACTEC 9240 blood culture bottles. Diagn Microbiol Infect Dis 1996;24:109-12.
22. Woods GL, LaTemple D, Cruz C. Evaluation of MicroScan rapid gram-positive panels for detection of oxacillin-resistant staphylococci. J Clin Microbiol 1994;32:1058-9.

=국문초록=

혈액 배양 양성 병에서 바로 실시하는 QMAC-dRAST의 그람 양성 구균에 대한 초고속 항생제 감수성 검사법의 임상 평가

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혈류 감염을 치료하기 위해서 필요한 항균제를 빠른 시간 내에 처방하는 것은 매우 중요하다. 초고속 항균제 감수성 검사는 감염 질환을 유발하는 원인균의 항균제의 감수성에 대한 빠른 판단을 할 수 있기 때문에 임상에서의 정확한 항균제 처방을 통한 치료를 가능하게 한다. 저자들은 그람 양성 구균이 포함된 115개의 혈액 배양 양성병(76개의 포도상구균, 39개의 장구균)을 QMAC-dRAST 시스템(Beckman Coulter, USA)을 이용하여 초고속 항균제 감수성 검사를 시행하였으며, 이를 MicroScan WalkAway 시스템(Quantamatrix Inc., Republic of Korea)을 대조군으로 선정하여 결과를 비교하였다. 13개의 항균제가 시험 대상에 포함되었으며, 두 시스템 사이의 일치율 및 불일치율을 도출하였다. 불일치한 경우에는 미량액체배지희석법에 의하여 후속 검증을 실시하였다. QMAC-dRAST 시스템은 94.9% (1,126/1,187)에 이르는 categorical agreement를 보였으며 1.0% (5/485)의 very major error, 1.3% (9/693)의 major error, 4.0% (47/1,187)의 minor error의 낮은 불일치율을 나타냈다. QMAC-dRAST 시스템은 MicroScan 시스템과 비교하였을 때, 그람 양성 구균에 대하여 빠른 시간 내에 정확하게 항균제 감수성을 검사하였으며, 이를 통해서 QMAC-dRAST 시스템이 의료 기관에서 조기에 정확한 진단에 필요한 필수 정보를 제공할 수 있을 것이라 기대한다. [Ann Clin Microbiol 2018;21:12-19]

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