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PATHOLOGY

Multi-center validation of the VITEK MS v2.0 MALDI-TOF mass spectrometry system for the identification of fastidious gram-negative bacteria

HARVARD MEDICAL SCHOOL

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Abstract

Background: Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) has recently been adapted for the rapid identification of cultured microorganisms. This technology could be especially advantageous if applied to fastidious bacteria, which can be difficult and time-consuming to identify using conventional methods. Here, we report the findings from a multi-center validation of the bioMérieux VITEK MS v2.0 system, which is designed for use in the clinical microbiology laboratory. **Methods:** The instrument's accuracy in identifying fastidious gram-negative bacteria was determined by comparison with nucleic acid sequence-based identification, using 226 unique clinical isolates. **Results:** Compared with the reference method, overall accuracy to the species level was 96% for fastidious, gram-negative bacteria. An additional 1% of isolates were correctly identified to the genus level: for these, the VITEK MS provided a split identification in which all the alternatives were from the same (correct) genus, allowing the user to deduce the genus with high confidence. One *C. jejuni* isolate was given the wrong species name (*C. coli*) without alternative identifications, although this species-level misidentification would have no clinical importance. There were no instances of a genus-level misidentification being provided as a single choice. The remaining isolates (3%) were each assigned split identifications with multiple genera among the alternatives, indicating poor discrimination, or an identification was not provided. **Conclusions:** The bioMérieux VITEK MS IVD instrument was highly accurate for the identification of fastidious gram-negative bacteria. Clinical laboratories can anticipate that a small fraction of such isolates will be unidentifiable by this method, necessitating alternative approaches. The ability to identify and rapidly report a specific identification for these bacteria will enhance the capabilities of many laboratories, and allow clinicians to use targeted therapy, which will aid antimicrobial stewardship.

Background

- MALDI-TOF mass spectrometry can be used to identify bacteria and other microorganisms in the clinical laboratory.
- Recent investigations have demonstrated that MALDI-TOF MS is a promising alternative to conventional methods for the identification of fastidious bacteria.
- There are currently no published reports on the performance of the VITEK MS v2.0 system (bioMérieux) for this application.

Methods

- Fresh bacterial isolates were obtained during the normal clinical workflow at five United States study sites; these were supplemented by frozen, archived isolates for less common species.
- Each isolate was analyzed by MALDI-TOF MS within 72 hours of visible growth in primary culture or subculture, after a minimum of 18 hours incubation under standard conditions.
- Bacterial colonies were directly applied to a single well of a target slide, overlaid with 1.0 µl of CHCA matrix, and air-dried prior to analysis.
- 16s rRNA gene sequencing using the MicroSeq system was used as the reference method. In the event of a low discrimination result, sequencing of alternative gene targets (*sodA* or *rpoB*) and/or phenotypic testing was performed.

Results

Table 1. Accuracy of the VITEK MS v2.0 system in the identification of fastidious gram-negative bacteria

Reference Method Identification	Number of isolates (fresh/frozen/sponsor)	VITEK MS Result				
		Single Identification Provided		Split Identification Provided		
		Accurate to species level (%)	Accurate to genus but not species level (%)	Alternatives are from same genus and genus is correct (%)	Alternatives are from multiple genera (%)	No Identification Provided (%)
Common Pathogens	**140**	**135 (96)**	**-**	**1 (<1)**	**3 (2)**	**1 (<1)**
Haemophilus influenzae	46/9/0	53 (96)	-	-	1 (2)	1 (2)
Legionella pneumophila	1/20/0	21 (100)	-	-	-	-
Moraxella (Branhamella) catarrhalis	17/16/0	33 (100)	-	-	-	-
Neisseria gonorrhoeae	5/12/12	26 (90)	-	1 (3)	2 (7)	-
Neisseria meningitidis	1/1/0	2 (100)	-	-	-	-
HACEK group	**43**	**40 (93)**	**-**	**1 (2)**	**2 (5)**	
Haemophilus parainfluenzae	23/10/4	34 (92)	-	1 (3)	2 (5)	-
Aggregatibacter actinomycetemcomitans	1/0/0	1 (100)	-	-	-	-
Aggregatibacter aphrophilus	1/0/0	1 (100)	-	-	-	-
Eikenella corrodens	4/0/0	4 (100)	-	-	-	-
Campylobacter species	**35**	**33 (94)**	**1 (3)**	**-**	**-**	**1 (3)**
Campylobacter jejuni	21/6/6	31 (94)	1 (3)*	-	-	1 (3)
Campylobacter coli	1/1/0	2 (100)	-	-	-	-
Others	**8**	**8 (100)**	**-**	**-**	**-**	**-**
Haemophilus parahaemolyticus	1/0/0	1 (100)	-	-	-	-
Neisseria cinerea	0/2/0	2 (100)	-	-	-	-
Neisseria mucosa	0/1/0	1 (100)	-	-	-	-
Oligella urethralis	2/2/0	4 (100)	-	-	-	-
Total	**226**	**216 (96)**	**1 (<1)**	**2 (<1)**	**5 (2)**	**2 (<1)**

*This *C. jejuni* isolate was identified as *C. coli* by the VITEK MS system.

Table 2. Split identifications provided by the VITEK MS v2.0 system

Reference Method Identification	VITEK MS Identification
H. influenzae	*H. influenzae, H. parahaemolyticus, Aerococcus viridans*
H. parainfluenzae	*H. parainfluenzae, H. influenzae*
H. parainfluenzae	*H. parainfluenzae, Micrococcus luteus/lylae*
H. parainfluenzae	*H. haemolyticus, Edwardsiella hoshinae*
N. gonorrhoeae	*N. gonorrhoeae, N. meningitidis*
N. gonorrhoeae	*N. gonorrhoeae, Trueperella bernardiae*
N. gonorrhoeae	*N. gonorrhoeae, Vibrio alginolyticus,*

Conclusions

- The VITEK MS v2.0 was highly accurate for the identification of fastidious gram-negative bacteria, compared with nucleic-acid sequencing as a reference method.
- The VITEK MS v2.0 provided a single, accurate, species-level identification for 96% of the study isolates.
- Clinical laboratories can anticipate that a small fraction of fastidious gram-negative bacterial isolates (3% in this study) will be unidentifiable using the VITEK MS v2.0 system, necessitating alternative approaches.