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Detection of Carbapenemase Producing Organisms by Matrix Assisted-Laser Desorption Ionization-Time of Flight Mass Spectrometry

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Introduction

Rapid, accurate diagnostic modalities for carbapenemase producing organisms (CPO) detection are needed. Matrix-Assisted Laser Desorption/Ionization Time-of-Flight mass spectrometry (MALDI-TOF MS) has been shown to accurately and quickly identify CPOs compared to traditional methods. In this study, we hypothesized that MALDI-TOF MS would accurately identify CPO with the following known mechanisms of resistance: KPC, VIM, NDM, IMI, IMP, OXA-48, and GES-16.

Methods

35 CPO, 3 beta-lactamases (GES-5, CMY-2, SHV-type ESBL) and 76 other non-carbapenemase producing organisms (nCPO) with no other known mechanisms of resistance were tested for carbapenemase production with microdilution, Etest[®], and MALDI-TOF MS. Degradation of any ertapenem specific peak (476 [M + H]⁺, 498 [M+ Na]⁺, and 520 [M + 2 Na]⁺) on MALDI-TOF MS was considered consistent with a CPO. MALDI-TOF MS results were compared to Etest[®], modified Hodge test, and microdilution (MicroScan [Beckman-Coulter] or Phoenix [Becton Dickinson]).

Results

All of the 76 nCPO had intact ertapenem peaks on MALDI-TOF MS. 2 of the nCPO, SHV-type ESBL *K.pneumoniae* and CMY-2 *C.freundii*, showed ertapenem degradation on MHT. 54.3% (19/35) of CPO

demonstrated degradation of all three ertapenem specific peaks on MALDI-TOF MS. 94.2% (33/35) of CPO demonstrated the absence of at least one peak. MHT identified 100% of CPOs but was also positive for 2/3 beta-lactamase producing nCPO. Microdilution of ertapenem, imipenem, and meropenem identified 94.3%, 97.1%, and 91.4% of CPOs, respectively. KPC-4 *K.pneumoniae* and IMP-18 *Ps.aeruginosa* were detected by MHT but not MALDI-TOF MS. Additional kinetic studies and sequence analysis are planned for these isolates. 1 of 3 KPC *E. cloacae* was not identified by MHT or microdilution and there was only degradation at the 520 peak on MALDI-TOF MS. Specificity of our assay was 100%.

Discussion

CPO detection is difficult and may require multiple methods for accurate detection. No method of detection identified all CPOs. MALDI-TOF MS requires minimal time for CPO detection with same day turn around. Procedures are also relatively simple and high-level training is not required. Establishing standard procedures and interpretations will be necessary for clinical use.