KPC Screening by Updated BD Phoenix and Vitek 2 Automated Systems

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Current BD Phoenix and Vitek 2 methodologies were assessed as screens for KPC β-lactamases. Using carbapenem MICs or expert system interpretations as screens, both systems exhibited high (97%) sensitivity in tests with 103 well-characterized Gram-negative isolates, 77 of which were KPC producers.

Pathogens producing carbapenemases of the KPC family are increasingly encountered and are typically associated with extensive multidrug resistance, leaving few to no therapeutic options (6, 10, 11). In 2009 the Clinical and Laboratory Standards Institute (CLSI) recommended carbapenemase screening for Enterobacteriaceae followed by confirmatory testing of screen-positive isolates (7). Emerging therapeutic outcome data indicate that carbapenem monotherapy for infections caused by KPC β-lactamase (KPC) and KPC producers is less reliable than combination therapy, and there is the risk of emergence of increased resistance if therapy is inappropriate (9, 10, 12, 13, 19). This supports the case for performing carbapenemase tests to identify pathogens against which carbapenem monotherapy may be unreliable. Initially, automated instruments were unreliable screens for KPC producers (1, 16), but since 2005 there have been modifications in the software and test panels to improve performance. The current study aimed to evaluate the most recent KPC screens (i.e., available in the United States in 2010) of the BD Phoenix (BD Diagnostics, Sparks, MD) and Vitek 2 (bioMérieux, Durham, NC) systems, by using susceptibility panels and software that are commercially available in the United States.

The isolates comprised 77 KPC-producing clinical isolates from hospitals in the United States and Puerto Rico and 26 clinically isolated KPC-negative isolates. β-Lactamases were characterized at Creighton University by previously published methods (14). The KPC producers were Klebsiella pneumoniae (n = 64), Klebsiella oxytoca (2), Escherichia coli (3), Enterobacter cloacae (4), and Pseudomonas aeruginosa (4). The enzymes were KPC-2 (9 isolates), KPC-3 (1), KPC-3-like (1), KPC-4 (3), KPC-8 (1), and KPC-like (62). “Like” indicates that the enzyme was confirmed as a KPC but not sequenced. The KPC-negative isolates included 7 producers of other carbapenemases (4 with class A carbapenemases and 3 with MBLs) and 19 producers of either a K1 β-lactamase, an extended-spectrum β-lactamase (ESBL), and/or an AmpC β-lactamase. These were K. pneumoniae (n = 5), K. oxytoca (2), E. coli (5), E. cloacae (5), Enterobacter aerogenes (1), Morganella morganii (1), Proteus mirabilis (2), Serratia marcescens (3), and P. aerugi- nosa (2). Inocula for both instruments were prepared from the same plate culture. The BD Phoenix panel, NMIC/ID-121, included ertapenem, imipenem, and meropenem. Its software version was V5.75A/V4.75A. The Vitek 2 card, AST-N142, included ertapenem and meropenem. Its software version was 04.02 PC. The reference standard for this study was the characterized β-lactamase status of the isolates. A reference MIC test was not included to assess the accuracy of automated MICs because of the known problem of variable MIC results with KPC producers (2–5, 15, 17). A positive screen comprised either a carbapenem MIC of ≥2 μg/ml or an expert system comment suggesting reduced carbapenem susceptibility or possible carbapenemase production.

Both instruments exhibited the greatest sensitivity by MIC screening, with 75 of the 77 KPC producers (97%) having a carbapenem MIC of ≥2 μg/ml (Table 1). Neither expert system improved KPC detection by yielding additional positive screens.

In BD Phoenix tests, ertapenem was the most sensitive screening agent (94% positive). Imipenem (48%) and meropenem (30%) were much less sensitive. Ertapenem in combination with either meropenem or imipenem provided maximum sensitivity (97%). The two falsely negative MIC screens were due to a KPC-4-producing E. coli strain and a P. aeruginosa strain that failed to grow in the susceptibility test. The expert system noted an elevated carbapenem MIC for 72 KPC producers (94%) and suggested possible carbapenemase production for 44 isolates (57%). Some expert interpretations could have been clearer. For example, ESBL production was reported as the resistance marker for most KPC producers, with a comment that ESBL production was confirmed and usually followed by a comment that varied from the bland “Enterobacteriaceae are usually susceptible to carbapenems....” to unambiguous suggestions of possible carbapenemase production. Since carbapenemases are clinically more important than ESBLs, the possibility of carbapenemase production could have been better emphasized to avoid the impression that ESBLs are more important.

In Vitek 2 tests, meropenem was a more sensitive screening agent (97% positive) than ertapenem (87% for all KPC producers and 92% for all non-P. aeruginosa KPC producers). Two KPC-4 producers were MIC screen negative; the E. coli isolate missed by the Phoenix and a K. pneumoniae isolate. The expert system noted an elevated carbapenem MIC for 68 KPC

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TABLE 1. Detection of KPC-producing strains

<table>
<thead>
<tr>
<th>Basis of analysis and category</th>
<th>No. (%) positive KPC-producing strains (n = 77) by:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BD Phoenix</td>
</tr>
<tr>
<td>MIC analysis</td>
<td></td>
</tr>
<tr>
<td>Any carbapenem MIC ≥ 2 μg/ml</td>
<td>75 (97)</td>
</tr>
<tr>
<td>Ertapenem MIC ≥ 2 μg/ml</td>
<td>72 (94)</td>
</tr>
<tr>
<td>Imipenem MIC ≥ 2 μg/ml</td>
<td>37 (48)</td>
</tr>
<tr>
<td>Meropenem MIC ≥ 2 μg/ml</td>
<td>23 (30)</td>
</tr>
<tr>
<td>Possible carbapenemase</td>
<td>44 (57)</td>
</tr>
</tbody>
</table>

*The results of 67/75 (92%) apply to Enterobacteriaceae only because the Vitek 2 test did not report ertapenem MICs for P. aeruginosa (no CLSI breakpoints for this drug/organism combination).

In conclusion, in this study the updated systems provided highly sensitive KPC screens. Screening based on a carbapenem MIC of ≥2 μg/ml (meropenem for Vitek 2; ertapenem in combination with either imipenem or meropenem for BD Phoenix) was most sensitive and less prone to misinterpretation than expert system screening. Both systems could be enhanced by improved expert system interpretations and the provision of carbapenemase confirmatory tests (18, 20).

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REFERENCES