Determining susceptibility patterns and prescribing behaviors related to a rapid diagnostic tool for Gram negative bacteremia

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BACKGROUND

- Verigene® is an automated microarray-based, multiplexed assay that can detect specific aerobic Gram positive (GP) and Gram negative (GN) bacteria along with certain antimicrobial resistance genes directly from positive blood culture bottles. Results are available within one to four hours.[1]
- Gram positive resistance markers definitively predict susceptibility to specific antimicrobials; therefore, utility in clinical practice is well-established and empiric treatment guidelines for GP results have been developed at Christiana Care Health System (CCHS).
- The GN panel identifies 8 GN organisms and 6 resistance genes.[2] All 6 genes encode for beta-lactamases, which are not all-inclusive of all beta-lactamases or other resistance mechanism that occur in GN bacteria (i.e. efflux pumps or porin channel changes).
- Although one recent study found prompt de-escalation and improved clinical outcomes after implementation of the Verigene® GN panel, the generalizability of their results is limited since prevalence of resistant isolates may differ between institutions.[5]
- For these reasons, development of institution-specific treatment guidelines for GN Verigene® results has yet to be achieved.

OBJECTIVES

PRIMARY OBJECTIVE

- Develop an antibiogram for each GN Verigene® result based on the final susceptibility pattern

SECONDARY OBJECTIVE

- Describe the prescribing patterns for patients with GN bacteremia post-implementation of Verigene®

OUTCOMES

PRIMARY OUTCOME

- Percent of each type of GN bacteria and resistance testing susceptible to an antibiotic.

SECONDARY OUTCOMES

- Percent of episodes in which antimicrobials were altered and the type of change that occurred (escalation, de-escalation, or lateral change), after receipt of Gram stain results, Verigene® results, and Vitek® or Sensititre® susceptibility results.

METHODS

STUDY DESIGN

- Retrospective, descriptive chart review at a large (>1,000 bed), community, teaching hospital

Inclusion Criteria	Exclusion Criteria
• ≥ 18 years of age • Admitted to CCHS between May 2015 through December 2015 • First episode of GN bacteremia identified by Verigene® with any result described in Table 1	• Expired prior to the availability of all results for the index blood culture • Polymicrobial infection • Pregnancy

RESULTS

Table 1. GN isolates and resistance markers detected by Verigene®

Isolates/Resistance Marker	N (%) Total N=168
Escherichia coli CTX-M	98 (58) 18/98 (18)
Klebsiella pneumoniae CTX-M	33 (20) 4/33 (12)
Pseudomonas aeruginosa	19 (11)
Proteus spp.	9 (5.5)
Klebsiella oxytoca	4 (2.5)
Enterobacter spp.	4 (2.5)
Acinetobacter spp. OXA	1 (0.5) 1/1 (100)
Citrobacter spp.	0
KPC, NDM, VIM, or IMP	0

Definitions

Empiric therapy: Antibiotic(s) administered at the time that the first blood culture was ordered, until Gram stain result is available

Gram stain guided therapy: Antibiotic(s) ordered after the Gram stain result is determined, before Verigene® result is available

Verigene® guided therapy: Antibiotic(s) ordered after Verigene® result and before susceptibilities are available

Definitive therapy: Antibiotic(s) ordered once the microorganism and susceptibilities (determined by Vitek®, Sensititre®, or other mechanism for susceptibility testing) are known

Escalation: Change in antimicrobial therapy with the intent to cover a broader spectrum of activity

De-escalation: Streamlining antibiotic therapy to cover a narrower spectrum of organisms

Lateral change: Switching an antibiotic to a different class with a similar spectrum of organisms

Susceptible: According to CCHS established breakpoints using the Clinical and Laboratory Standards Institute for 2015

Table 2. Antibiogram based on susceptibilities of Verigene® -detected GN isolates/resistance markers, Total isolates (%Susceptible)

	Amp/Sul	Pip/tazo	Cefazolin	Ceftriax	Cefepime	Aztreon	Cipro/ Levo	Mero	Amikacin	Gent/ Tobra	Tigecycline	TMP/SMX
E. coli No resistance	80 (56)	80 (95)	80 (75)	80 (98)	80 (100)	79 (99)	80 (80)	79 (100)	80 (100)	80 (94)	79 (100)	80 (73)
E. coli CTX-M	18 (17)	18 (94)	18 (0)	18 (0)	18 (0)	18 (0)	18 (0)	18 (100)	18 (100)	18 (44-56)	18 (100)	18 (33)
K. pneumoniae No resistance	29 (97)	29 (100)	29 (97)	29 (97)	29 (97)	29 (97)	29 (100)	29 (100)	29 (100)	29 (75-100)	29 (97)	29 (93)
K. pneumoniae CTX-M	4 (0)	4 (75)	4 (0)	4 (0)	4 (0)	4 (0)	4 (25-50)	4 (100)	4 (100)	4 (0-100)	4 (50)	4 (0)
K. oxytoca No resistance	4 (75)	4 (100)	4 (25)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)
Proteus spp. No resistance	9 (100)	9 (100)	9 (78)	9 (100)	9 (100)	9 (100)	9 (100)	9 (100)	9 (100)	9 (100)	9 (0)	9 (89)
Enterobacter spp. No resistance	N/A	4 (100)	4 (0)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)
P. aeruginosa No resistance	N/A	19 (100)	N/A	N/A	19 (100)	19 (100)	19 (95)	19 (100)	19 (100)	19 (100)	N/A	N/A
Acinetobacter spp. OXA	1 (0)	1 (0)	N/A	1 (0)	1 (0)	N/A	1 (0)	1 (0)	1 (0)	1 (0)	1 (100)	1 (0)

Abbreviations: amp/sul = ampicillin/sulbactam, pip/tazo = piperacillin/tazobactam, ceftriax = ceftriaxone, aztreon = aztreonam, cipro = ciprofloxacin, levo = levofloxacin, mero = meropenem, gent = gentamicin, tobra = tobramycin, tmp/smx = trimethoprim/sulfamethoxazole

RESULTS (Continued)

Figure 1. Occurrence of therapy changes related to blood culture testing results

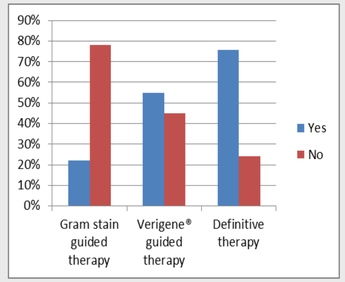
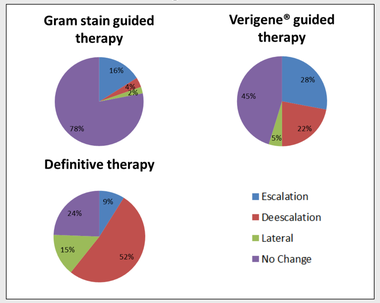


Figure 2. Prescribing patterns related to blood culture testing results



CONCLUSIONS

- Limitations of this study include: retrospective chart review, the small number of isolates/resistance markers other than *E.coli* limit the applicability of these results in clinical practice until additional data is collected, unable to determine additional types of GN resistance and their effect on susceptibilities, inability to capture true motives for prescribing behavior other than blood culture testing results (i.e. changes in clinical status or concern for additional infection), exclusion of polymicrobial infections
- The results of this study have enabled the Antimicrobial Stewardship Program (ASP) at CCHS to guide empirical antibiotic therapy for select GN Verigene® results prior to availability of susceptibility testing
- At CCHS, ceftriaxone is appropriate for *E.coli* isolates not expressing CTX-M, whereas penicillin allergic patients should receive aztreonam instead of a fluoroquinolone
- Carbapenems should be reserved for isolates expressing CTX-M; reporting has been updated to recommend a carbapenem as preferred therapy when CTX-M is detected
- Implementation of the GN Verigene® platform has impacted prescribing patterns for patients with GN bacteremia, which may lead to patients receiving more targeted therapy sooner; however, there may be opportunity to promote further de-escalations based on Verigene ® results instead of waiting for final susceptibility results

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DISCLOSURE

Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

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