An Antibiotic Stewardship Program (ASP) blueprint for optimizing Verigene BC-GN within an institution: A tale of two cities

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Background

- Rapid diagnostic tests (RDTs) have shown the ability to decrease the time to appropriate therapy in patients with bloodstream infections (BSIs), leading to decreases in both mortality and length of stay for survivors
- Verigene (Luminex Corp, Austin, TX, USA) has two RDT platforms for bacterial BSIs: Gram-positive (Verigene BC-GP) or Gram-negative (Verigene BC-GN)
- Verigene BC-GN detects four organisms to the genus level and four to the species level (with US/FDA cleared platform) along with the presence/absence of six problematic beta-lactamase genes (CTX-M, KPC, VIM, IMP, NDM, OXA)
- When a given beta- lactamase gene is present, antibiotic stewardship personnel can escalate therapy, minimize time to appropriate therapy, and improve patient outcomes
- However, given the complexity of Gram-negative resistance, antibiotic stewardship teams are left without clear direction for intervention when an organism is detected in the absence of resistance genes
- This often results in broad empiric therapy based on local antibiogram data to ensure coverage of the detected pathogen
- The primary objective of this analysis was to determine the ability of Verigene BC-GN genus/species results and beta- lactamase positivity/negativity to predict antimicrobial susceptibility among target GN organisms in order to better direct antimicrobial stewardship programs

Methods

Retrospective review of all blood cultures positive for Gram-negative (GN) bacteria at the Detroit Medical Center (DMC) and University of Maryland Medical Center (UMMC)
June 2015 – July 2016

Both DMC and UMMC have adopted Verigene BC-GN at their sites and isolates were run on equipment as part of routine laboratory diagnostic workup

Compare results of Verigene BC-GN with those of conventional antimicrobial susceptibility testing at each institution

Determine sensitivity, specificity, positive, and negative predictive value of presence/absence of beta-lactamase genes and antimicrobial susceptibility to target antimicrobials both in aggregate and per institution

Results: Detroit Medical Center

Organism	N	Target antimicrobial	Resistance marker	Number Resistant	Percent Resistant	Number picked up by test	Sens	Spec	PPV	NPV
E. coli	384	Ceftriaxone	Any	63	16	56	89	99	97	98
K. pneumoniae	140	Ceftriaxone	Any	39	28	33	85	99	97	94
		Ertapenem	KPC	7	5	6	86	100	100	99
Proteus spp.	57	Ceftriaxone	Any	7	12	4	57	100	100	94
Acinetobacter spp.	39	Meropenem	OXA	10	26	8	80	93	80	93
P. aeruginosa	51	Cefepime	Any	6	12	0				88
K. oxytoca	23	Ceftriaxone	Any	2	9	1	50	100	100	95
Enterobacter spp.	61	Cefepime	Any	3	5	1	33	100	100	97
Citrobacter spp.	10	Cefepime	Any	0	0	0				100

Results: University of Maryland Medical Center

Organism	N	Target antimicrobial	Resistance marker	Number Resistant	Percent Resistant	Number picked up by test	Sens	Spec	PPV	NPV
E. coli	106	Ceftriaxone	Any	16	15	14	89	99	94	98
K. pneumoniae	58	Ceftriaxone	Any	16	28	12	80	100	100	91
		Ertapenem	KPC	5	9	5	100	98	83	100
Proteus spp.	12	Ceftriaxone	Any	0	0	0				100
Acinetobacter spp.	14	Imipenem	OXA	5	36	5	100	100	100	100
P. aeruginosa	43	Piperacillin-tazobactam	Any	15	35	0				65
K. oxytoca	9	Ceftriaxone	Any	0	0	0				100
Enterobacter spp.	33	Cefepime	Any	3	9	3	100	100	100	100
Citrobacter spp.	6	Cefepime	Any	0	0	0				100

Sample Antibiograms

DMC		Verigene Isolates July 2015- June 2016 - % Susceptible										
Organism	N	SAM	TZP	CZO	CRO	FEP	FOX	ETP	MEM	GEN	CIP	ATM
***E. Coli* (none)**	326	52	99	75	98	99	94	100	100	92	82	99
***E coli* CTX-M**	58	5	84	0	3	22	94	100	100	48	5	10
***Klebsiella pneumoniae* (none)**	106	83	97	84	94	99	88	100	100	94	94	93
***Klebsiella pneumoniae* CTX-M**	28	0	57	0	4	4	68	96	100	46	36	25

SAM: ampicillin/sulbactam; TZP: piperacillin/tazobactam; CZO: cefazolin; CRO: ceftriaxone; FEP: cefepime; FOX: cefoxitin; ETP: ertapenem; MEM: meropenem; GEN: gentamicin; CIP: ciprofloxacin; ATM: aztreonam

UMMC	Verigene Isolates September 2015- June 2016 - % Susceptible											
Organism	N	SAM	TZP	CZO	CRO	FEP	ETP	MEM	GEN	LVX	SXT	ATM
E. Coli (none)	92	44	88	82	99	99	100	100	84	71	69	100
***E. coli* CTX-M**	14	21	93	0	0	0	99	100	29	21	36	0
***Klebsiella pneumoniae* (none)**	45	80	93	84	91	100	100	100	98	100	84	86
***Klebsiella pneumoniae* CTX-M**	7	0	43	0	0	14	100	100	57	43	14	0

SAM: ampicillin/sulbactam; TZP: piperacillin/tazobactam; CZO: cefazolin; CRO: ceftriaxone; FEP: cefepime; ETP: ertapenem; MEM: meropenem; GEN: gentamicin; LXV: levofloxacin; SXT: trimethoprim/sulfamethoxaole; ATM: aztreonam

Conclusions

- Susceptibility to target antimicrobials was largely predicted by absence of beta- lactamase genes at both institutions
  - A notable exception was *P. aeruginosa* where, given the complex nature of beta-lactam resistance, none of the resistant isolates were predicted by Verigene BC-GN
- As NPV are >90% for all other bug/drug combinations stewardship personnel at each institution should feel comfortable recommending definitive therapy (escalation and de-escalation) at each site based on Verigene BC-GN results
- Given known geographical variations in antimicrobial resistance, other institutions should NOT utilize our data at their institution.
  - However, our data show that institution specific guidelines can be developed to guide treatment decisions, including de-escalation opportunities, based on Verigene BC-GN results
- This simple process displays a blueprint that ASPs can perform at their institutions to optimize use of Verigene GN-BC for GN BSIs

Disclosures: JKJ, HS, and PL have received grant support for other research from Nanosphere, all others have no disclosures