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Abstract

Background MRSA is a significant cause of both health-care associated and community-associated infections. VAN has been the mainstay of parenteral therapy for MRSA infections. However, its efficacy has come into question, with concerns over its poor tissue penetration, slow bactericidal activity, and possible "MIC creep" among susceptible strains. We sought to assess national trends in management of adult infections due to MRSA and reports of both MRSA VAN MIC creep and clinical failures with VAN use.

Methods Electronic 12-question survey of adult ID physician members of the IDSA Emerging Infections Network was conducted from 11/18/2015 to 12/18/2015.

Results 652 (53%) physicians responded, of whom 617 treat *S. aureus* infections. Of these, 95% reported their clinical micro lab used a breakpoint of ≤ 2 µg/mL as indicative of MRSA susceptibility to VAN; 91% reported routine inclusion of the MIC in the susceptibility report. VAN MICs were determined via E-test by 18%, broth microdilution 3%, Vitek 38%, Microscan 25%, BD Phoenix 6%; 14% were unsure of method used. 21% reported vancomycin treatment failure with MRSA bacteremia despite adequate troughs and source-control at least once over the last year; 50% reported ≥2 times. 37% of these reported initial MIC <2 µg/mL and 22% MIC=2 in their most recent treatment failure. VAN was the empiric treatment of choice for persons who inject drugs and right-side IE in 89% (509/572) followed by daptomycin, 5% (29/572); 53% would switch from VAN to alternate therapy if MIC=2 µg/mL; 6% would continue treatment with VAN at same dose despite 4 d of persistent bacteremia.

Conclusions 59% of respondents reported initial VAN MICs ≤ 2 µg/mL with persistent MRSA bacteremia, while VISA and VRSA were rarely encountered (MIC>2 µg/mL, 2%), reflecting poor response to therapy at the higher end of the CSLI susceptibility-range. This may partially be due to resistance-undercall of certain testing methods. Nonetheless, VAN's poor therapeutic efficacy at MIC ≤ 2 µg/mL across a wide geographic distribution renders "MIC creep" more probable than clonal spread or testing artifact. Elevated MRSA VAN MICs have been associated with elevated daptomycin MICs, rendering the latter potentially problematic as alternate therapy.

Introduction

- MRSA frequently causes invasive infections with overall annual US 2012 incidence at 23.99/100,000.[1]
- Vancomycin is the primary parenteral agent for treating MRSA, but strains with decreased susceptibility to vancomycin (MIC 4-8) and resistance (MIC>=16) have been reported since 1996.[2,3,4]
- Other concerns with vancomycin include: slow bactericidal activity and possible "MIC creep" among susceptible strains.[2,3,4]
- IDSA 2011 clinical practice guidelines for the treatment of MRSA infections in adults and children address issues related to the use of vancomycin therapy in the treatment of MRSA infections, including dosing and monitoring, current limitations of susceptibility testing, and the use of alternate therapies for patients with vancomycin treatment failure and infection due to strains with reduced susceptibility to vancomycin.

Aim

- To assess national trends in management of adult infections due to MRSA and reports of both MRSA VAN MIC creep and clinical failures with VAN use.

Methods

- Electronic 12-question survey of adult ID physician members of the IDSA Emerging Infections Network was conducted from 11/18/2015 to 12/18/2015.
- Descriptive statistics were calculated using SAS 9.4 (Carey, NC)

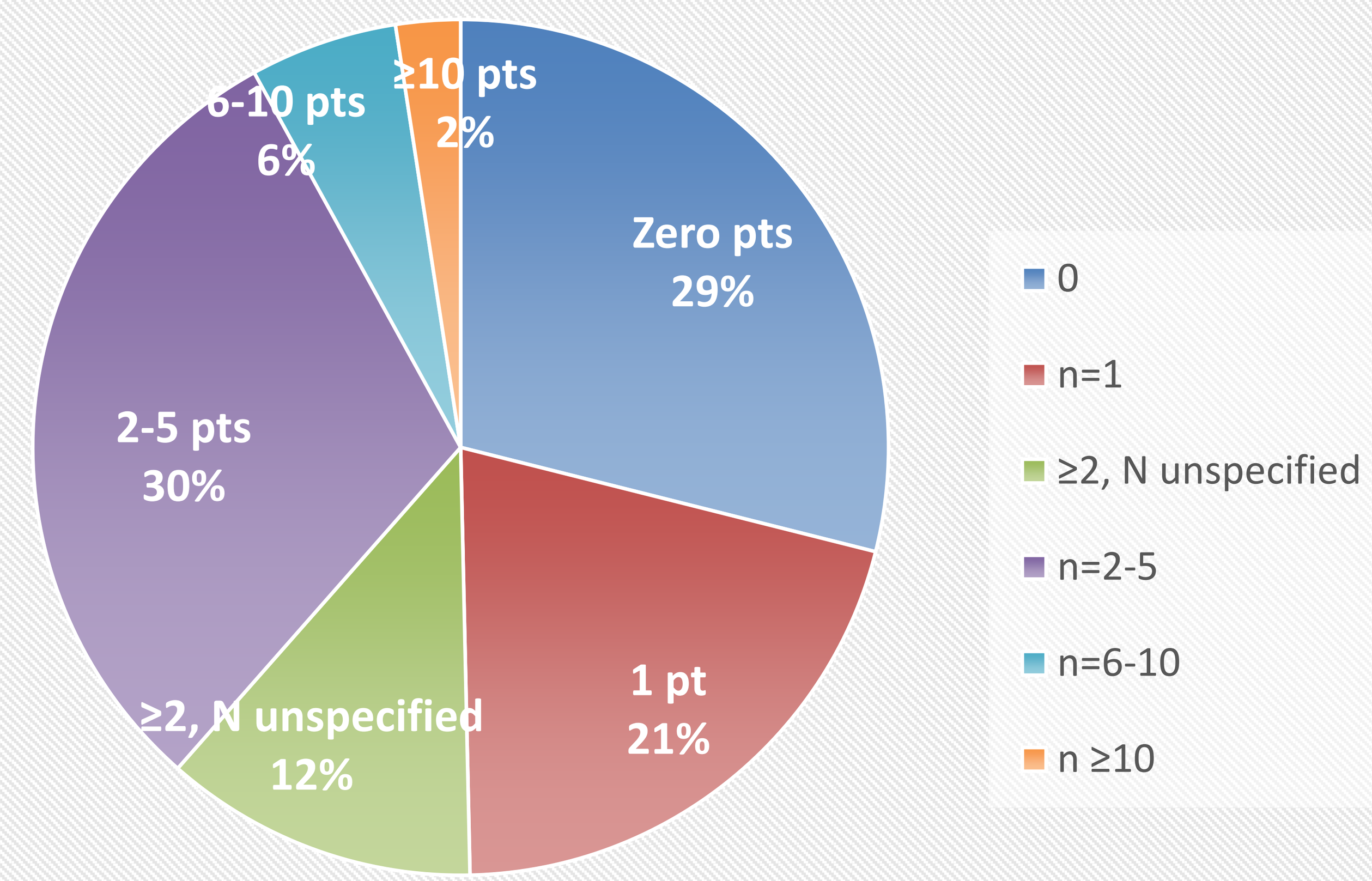
Study Population

- 652/1,232 (53%) EIN member physicians w/ an adult infectious diseases practice responded.
- The study sample was diverse in terms of respondent geography, experience & employment (Table 1).
- 617/652 (94%) treat pt(s) with *S. aureus* infection
- 587/617 (95%) report MRSA VAN breakpoint used by their clinical micro lab as 2 µg/ml.
- 562/617 (91%) report that the measured MIC of VAN is included in their susceptibility reports.

Table 1.	# respondents/category (%)
US Census Bureau Regions	
NE	161/268 (60)
MW	167/310 (54)
South	181/346 (52)
West	136/290 (47)
Canada	6/15 (40)
Years of Experience	
<5	153/269 (57)
5-14	173/416 (42)
15-24	146/256 (57)
≥25	180/ 291(62)
Employment	
Hospital/clinic	198/371 (53)
Private/group practice	205/366 (56)
University/medical school	207/417(50)
VA and military	40/71 (56)
State Govt	2/7 (29)

Results

Figure 1: Number of patients with persistent MRSA bacteremia (>6 days on VAN) encountered in last 12 months; 574 respondents



Most recent initial MRSA VAN MIC encountered; 574 respondents

- <2 µg/ml: 214 (37%)
- 2 µg/ml: 127 (22%)
- >2 µg/ml: 11 (2%)
- Don't remember: 56 (10%)
- Not applicable (0 encountered): 166 (29%)

In IVDU pts with tricuspid valve IE and positive blood cultures for *S. aureus*, preferred initial empiric therapy choice:

- Ceftaroline: 4 (0.7%)
- Daptomycin: 29 (5%)
- Linezolid/tedizolid: 1 (0.2%)
- Telavancin: 1 (0.2%)
- **Vancomycin: 509 (89%)**
- Other: 28 (5%)

Blood isolate reported as MRSA with VAN MIC = 2µg/ml in febrile IVDU pt with tricuspid valve IE on VAN day 2:

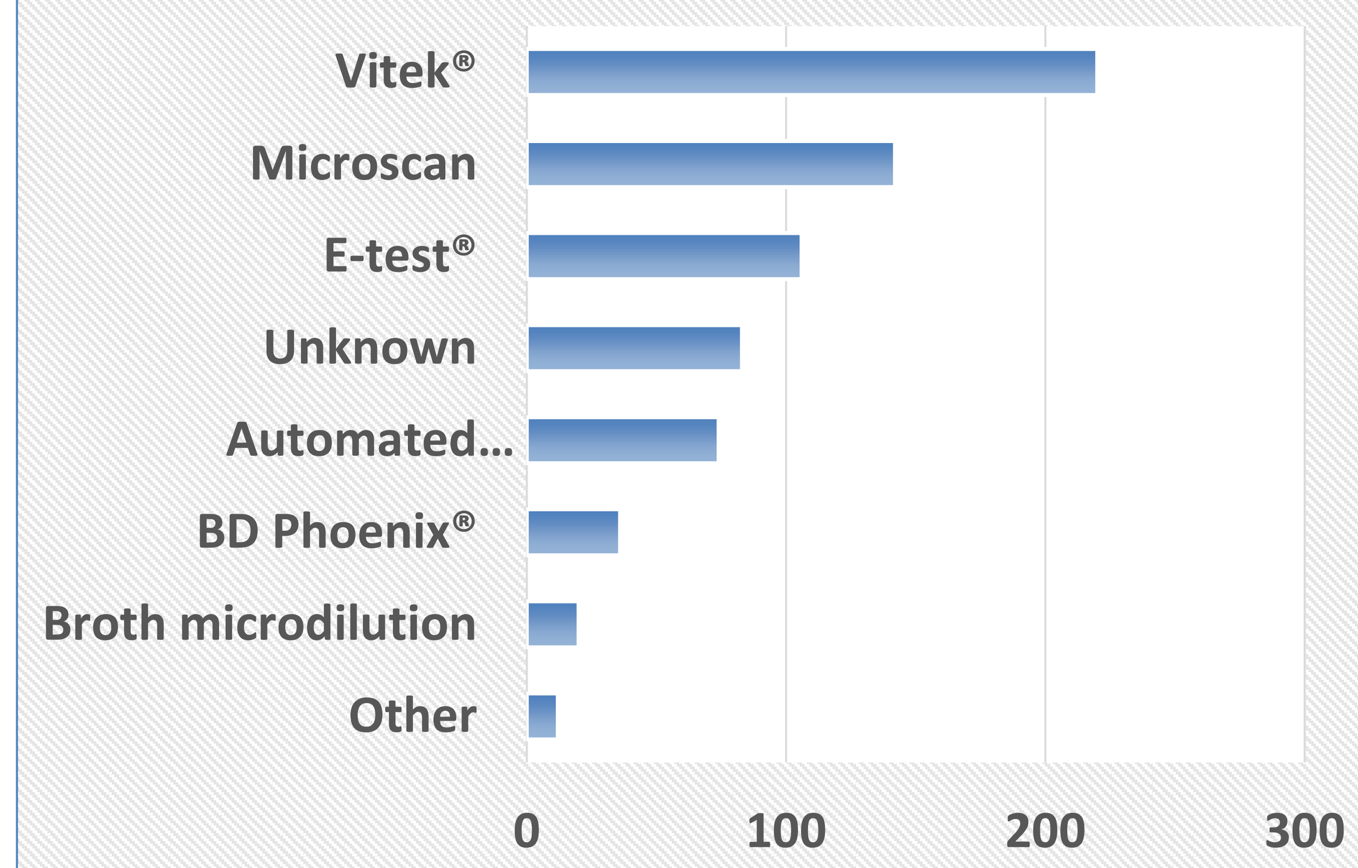
- Ceftaroline: 32 (6%)
- **Daptomycin: 310 (54%)**
- Linezolid/tedizolid: 9 (2%)
- Telavancin: 2 (0.3%)
- **Continue Vancomycin: 213 (37%)**
- Other: 7 (1%)

Six days later, pt remains febrile and blood cultures from day 4 with MRSA, VAN MIC=2 on VAN therapy:

- Ceftaroline: 76 (13%)
- **Daptomycin: 360 (63%)**
- Linezolid/tedizolid: 11 (2%)
- Telavancin: 5 (0.9%)
- **Continue Vancomycin, same dose: 35 (6%)**
- Continue Vancomycin, higher dose: 13 (2%)
- Combination therapy: 69 (12%)

•ceftaroline + daptomycin (36), daptomycin + rifampin (8), vancomycin + ceftaroline (5), daptomycin + β-lactam (nafcillin) (4), vancomycin + gentamicin (3), vancomycin + rifampin (3), daptomycin + gentamicin (1).

Figure 2. MRSA VAN MIC: Clinical Laboratory Methods – # using



574 respondents; ≥1 answer permitted, numbers add up to more than 100%

Conclusions

- Vancomycin is still the preferred drug for treating right sided endocarditis due to MRSA, which probably is a good measure of how physicians treat deep MRSA infections.
- Poor therapeutic response and persistent bacteremia despite 6 days of vancomycin were surprisingly common, being seen at least two times annually by 50% of respondents.
- Even though VISA and VRSA were rarely encountered, MIC's at the upper limit of susceptibility were being seen and, in the presence of clinical failure, often caused the physician to switch to daptomycin or another drug or combination.

References

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