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Vancomycin Experience in Physician Office Infusion Centers

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Abstract

Background: Vancomycin (VAN) has been used in physician office infusion centers (POICs) in patients (pts) with a variety of gram-positive infections. The assessments of patients in the POIC setting may allow for optimal monitoring of outpatient VAN therapy and early recognition of adverse events. We describe the clinical course of pts treated with vancomycin in POICs.

Methods: The medical records were queried of the first 25 pts from 4 POICs that treated pts with VAN during June to December, 2012. Data included demographics, diagnosis, organisms, pertinent laboratory data, assessment of creatinine clearance, therapy regimen, adverse events, and clinical outcomes. Therapeutic range for VAN was defined as 15-20 mg/dL. Clinical success was defined as cure or improved. Cure was defined as resolution of disease and negative laboratory results when available. Improved was defined as partial resolution with continuation of oral antibiotics or other intervention.

Results: 100 patients were evaluated. 51 pts were female; mean age was 56 years (range 6-78). Infections included 52 complicated skin and soft tissue, 26 bone and joint, 11 blood stream infection, 7 respiratory infections, 2 intra-abdominal infection, and 2 urinary tract infections. Mean initial VAN dose was 13.7 mg/kg (range 7.3-31.4). Mean length of therapy was 24 days (range 4-88). Culture data was available in 75 pts with several mixed infections. Predominant pathogens included 44 methicillin-resistant *Staphylococcus aureus* and 13 coagulase-negative staphylococci. 99 pts had at least 2 serum creatinine (SCR) levels for comparison. 82 pts had at least 2 VAN troughs for comparisons. 2 pts had an increase in SCR of 0.5 mg/dL or more; 1 pt had an elevated VAN trough. Overall VAN clinical treatment success was 82%, with 56 cured and 26 improved. 7 pts failed and switched therapy due to adverse events, including neutropenia, eosinophilia, respiratory distress, increased SCR, myalgia, nausea, and rash/itching. 11 were non-evaluable for VAN therapy, 5 for transfer of care, 4 for therapy change due to culture results and 2 for clinical preference.

Conclusion: VAN was used for a variety of infections in POIC with positive outcomes and few adverse events experienced by pts requiring discontinuation. VAN appears to be an effective and well-tolerated therapy in POICs.

Introduction

Parenteral vancomycin has been used in the inpatient setting for many decades to treat a variety of Gram positive infections. In the last decade, interest has expanded in using parenteral vancomycin in the outpatient setting to continue treatment for patients who require longer duration of therapy, to initiate therapy for patients who are otherwise stable and do not require hospitalization, and to transition patients who require parenteral therapy to the most appropriate level of care.[1] The physician office infusion center (POIC) assessments may also allow for ideal management of patients and prevention or early recognition of adverse events.

Methods

Patients receiving parenteral vancomycin during June through December 2012 were identified in 4 POICs. The medical records of the first 25 patients at each site were queried and data were collected. Data collected included gender, age, height, weight, comorbidities, serum creatinine, complete blood count with differential, culture results, treatment regimen and changes thereto, infection type and location, presence of prosthetic material, serum vancomycin concentrations, patient outcomes, adverse events, and reason for discontinuation of therapy. Ideal body weight was calculated, body mass index was calculated, dose in mg/kg based on total body weight was calculated, and creatinine clearance was calculated using Cockcroft-Gault equation for adults and Schwartz equation for pediatrics. The therapeutic range for vancomycin trough concentrations was defined as 15-20 mg/dL. Nephrotoxicity was defined as an increase of 0.5 mg/dl or more from baseline during the therapy course. Patient outcomes were defined as cured, improved, failed, or non-evaluable. Cured was defined as resolution of disease and resolution of previously abnormal laboratory results. Improved was defined as partial resolution of disease with continuation of oral antimicrobials or other intervention. Failed was defined as patient signs and symptoms not resolving or worsening or patients requiring switching from vancomycin for AEs. Clinical success was defined as cured or improved. Data was divided into patients who had antibiotics initiated in hospital and were transitioned to POIC and patients who were initiated in the POIC. Comparisons were made between these groups using Fisher's exact test for categorical data and student's t-test for variance.

Results

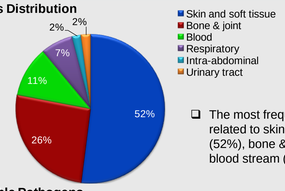
Demographics

Characteristics	Hospital to POIC (n=52)	POIC Only (n=48)	Total (n=100)	p Value*
Gender				
Female	22	29	51	0.433
Age in years				
Mean (range)	57 (6-78)	55 (26-78)	56 (6-78)	1
≥ 65	14	11	25	0.81
Mean weight in kg (range)	93 (25-171)	92 (50-197)	93 (25-197)	0.5
Mean BMI (range)	30.6 (16.0-62.3)	31.4 (19.8-56.5)	30.6 (16.1-62.3)	1
≥ 30	26	22	48	0.69
Comorbidities				
Hypertension	26	23	49	0.84
Obesity	26	22	48	0.69
Diabetes mellitus	22	18	40	0.68
Cardiovascular disease	13	8	21	0.33
Depression/anxiety	15	7	22	0.09
Asthma/COPD	6	9	16	0.4
Cancer	7	5	12	0.76
Hyperlipidemia	5	5	10	1
Comorbidities per patient				
0	6	2	8	0.27
1	7	10	17	0.42
2	8	12	20	0.31
≥3	31	24	55	0.42
Reported prosthetic device	7	1	8	0.06
Mean baseline SCr in mg/dL (range)	0.9 (0.4-1.4)	0.9 (0.5-2.8)	0.9 (0.4-2.8)	1

- Gender was equally distributed among all pts.
- Over half of all pts had 3 or more comorbidities, 40% of which included diabetes and nearly 50% with HTN and obesity.
- Demographics were similar between previously hospitalized pts *versus* POIC only treated pts.

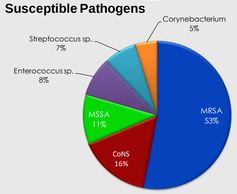
Diagnosis and Pathogens

Diagnosis Distribution



- The most frequent infections were related to skin and soft tissue (52%), bone & joint (26%), and blood stream (11%).

Susceptible Pathogens



- 83 vancomycin-susceptible organisms were identified in 75 pts.
- MRSA was report in 44 pts and the primary organism in over half.
- CoNS was the second most prevalent in 13 pts.
- Confirmed or suspected staph was noted overall in 63% of pts.
- 6 pts had gram negative organisms also identified.

Type of Infection with Mixed Pathogens	No. of Patients
Skin and soft tissue	9
Bone and joint	4
Blood stream	1
Respiratory	1
Urinary tract	1

- 16 pts had polymicrobial infections, most often with cellulitis and abscess

Vancomycin Treatment Characteristics

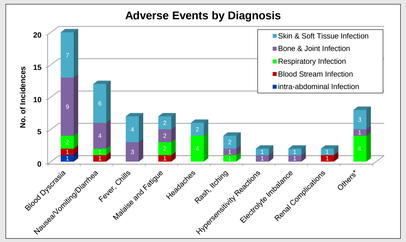
Characteristics	Hospital to POIC (n=52)	POIC Only (n=48)	Combined (n=100)	p Value*
Mean Initial Dose (mg/kg)				
Skin and soft tissue	13.5	11.6	12.7	0.96
Bone and joint	15.6	14.3	15.0	0.95
Blood stream	16.3	10.6	15.2	0.98
Respiratory	–	13.5	13.5	–
Intra-abdominal	27.5	13.6	10.5	0.99
Urinary Tract	–	11.0	11.0	–
Total (range)	**14.8 (7.3-31.4)**	**12.6 (7.6-20.4)**	**13.7 (7.3-31.4)**	1
Median LOT (days)				
Skin and soft tissue	18	14	15	1
Bone and joint	25	36	36	0.94
Blood stream	14	9	10	0.87
Respiratory	–	39	39	–
Intra-abdominal	10	28	19	1
Urinary Tract	–	12	12	–
Total (range)	**21 (7-88)**	**17 (4-54)**	**21 (4-88)**	1
Renal function				
Baseline serum creatinine (mg/dL)	0.91 (0.4-2.2)	0.98 (0.5-2.8)	0.93 (0.4-2.8)	0.45
Increase of >0.5 mg/dL in SCr, No. (range)	4 (0.6-1.84)	0	4 (0.6-1.84)	0.12
Mean CrCl at start of therapy (mL/min)	90.7 (45-164.5)	81.6 (19-141.6)	86.3 (19.164.5)	0.5
Mean CrCl at completion of therapy (mL/min)	78.8 (53-139)	76.0 (58-100)	78.2 (53-139)	0.5
Mean change (+/-) per patient (range) (mL/min)	0.28 (-69 to 70)	4.6 (-89 to 49)	2.4 (-89 to 70)	0.5
Therapeutic troughs (15-20 mg/dL), No. (%)	55 (31%)	40 (29.4%)	95 (30.2%)	0.88
Troughs (10-20 mg/dL), No. (%)	110 (61.4%)	92 (67.6%)	202 (64.1%)	0.29
Median No. of troughs per patient	3 (1-6)	2 (0-9)	3 (0-9)	0.25
Median VAN trough levels (mg/dL)				
Baseline	14.0 (5-45.9)	N/A	–	–
1st Week	16.4 (5-34.0)	11.8 (3.5-23.5)	11.9 (3.5-34)	1
2nd Week	14.5 (5.7-29.2)	13.8 (3.8-20.6)	13.8 (3.8-29.2)	0.91
3rd Week	16.8 (7.8-28.8)	15.9 (10.3-22.6)	15.9 (7.8-28.8)	0.93
4th Week	17.1 (9-23.8)	15.8 (9-21.7)	15.6 (9-23.8)	0.95
5th Week	15.6 (10.8-27)	15.6 (11.8-29.4)	15.8 (10.8-29.4)	1
6th Week	–	15.9	–	–
7th Week	–	17.1	–	–
Overall (range)	**15.7 (5-45.9)**	**15.8 (3.5-23.5)**	**15.7 (3.5-29.4)**	0.25

*: Student's t-test, Fisher's exact

Safety

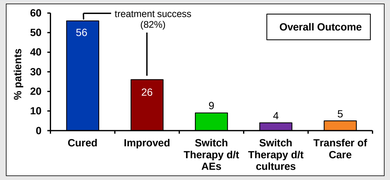
Significant Adverse Events	Hospital to POIC No.	Associated with Elevated Trough No. (%)	POIC Only No.	Associated with Elevated Trough No. (%)	Combined No.	Associated with Elevated Trough No. (%)	p value
Neutropenia	6	2 (33)	5	1 (20)	11	3 (27)	*1/1
Thrombocytopenia	3	2 (67)	4	3 (75)	7	5 (71)	0.71/1
Nephrotoxicity†	4	1 (25)	–	–	4	1 (25)	NA
Electrolyte Disturbance	2	1 (50)	–	–	2	1 (50)	NA
Hypersensitivity Reaction	2	1 (50)	–	–	2	1 (50)	NA
Eosinophilia	1	1 (100)	1	1 (100)	2	2 (100)	*1/1
Total	18	8 (44)	10	5 (45)	28	13 (28)	*1/1

†Defined as increase in serum creatinine of ≥0.5 mg/dL from baseline during therapy; *Fisher's exact test: hosp vs POIC/POIC vs. total.

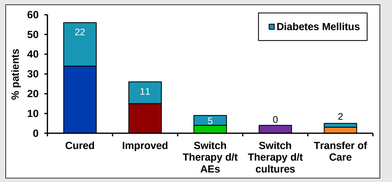


* Other adverse events reported include dizziness (3), decreased appetite (2), edema (1), myalgia (1), and yeast infection (1).

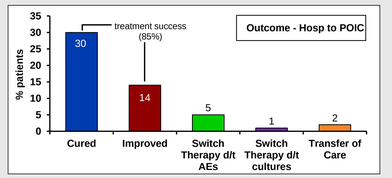
Outcomes

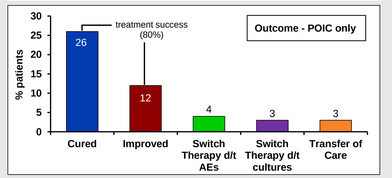


- 82 pts had a successful outcome while on VAN therapy.
- 9 pts experienced adverse events and were switched to antimicrobials other than VAN.
- 4 pts were switched to antimicrobials other than VAN due to culture results.
- 5 pts were transferred to other care centers such as hospitals (n=3), home health care (n=1), and rehabilitation facility (n=1).



- Among the above data, the following number of pts were diabetics:
  - 22/56 pts with cured and 11/26 pts with improved outcomes
  - 5/9 pts who switched VAN therapy due to AEs
  - 2/5 pts who underwent transfer of care.





- Successful outcomes were seen in both groups at 85% and 80%, respectively, with few differences in the groups.
- Therapy switches due to AEs were similar in both groups. More patients were switched following culture results in the POIC only treatment group.

Discussion

- Clinical treatment success was noted in 82% of pts. Pts who had therapy initiated in the POIC had similar outcomes to pts receiving therapy following hospital discharge.
- 30% of pts overall had therapeutic troughs of 15-20 mg/dl. 64% of pts had troughs between 10 and 20 mg/dl. Overall, median troughs were 15.7 mg/dl and similar in both groups.
- Adverse events leading to vancomycin discontinuation were minimal (7%) with no long term sequelae.
- 32 pts (23 and 9 in Hosp *vs.* POIC group, respectively) had elevated vancomycin trough levels throughout the course of therapy. Of these, elevated trough levels were associated with significant adverse events in 28 pts (88%) with 18 Hosp, 10 POIC.
  - Neutropenia, thrombocytopenia and eosinophilia occurred most often in pts with elevated vancomycin troughs.
  - Four pts experienced an increase in serum creatinine of ≥0.5 from baseline during therapy. One was associated with an elevated trough of 29.7, which resulted in acute renal injury.
- Of the 39 pts with reported AEs, 19 were cured, 11 improved, 7 were switched to other agents, and 2 were non-evaluable.

Conclusions

- Vancomycin may be safely initiated in a POIC and is a safe and effective drug for continued use in this setting.
- Different types of infections can be safely treated with vancomycin in the POIC
  - Bacteremia
  - Pulmonary
  - Bone and joint
  - Skin and soft tissue
  - Urinary tract infection
  - Intra-abdominal infections
- Appropriate monitoring can be accomplished in the POIC including laboratory studies.
- Our data demonstrates a low rate of adverse events, rarely leading to alterations in therapy, even with trough levels between 15-20 mg/dl.
- Leukopenia and thrombocytopenia, as opposed to the traditional concerns of acute kidney injury, were the most notable side effects. Thus, routine complete blood count monitoring is important.
- Outcomes in both the POIC initiated treatments and the hospital transition to POIC treatments were impressive.

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