A Safety analysis of High Dose Intrawound Vancomycin in Arthroplasty

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INTRODUCTION

- The prevention of periprosthetic joint infections (PJI) is of upmost importance given the significant morbidity and mortality associated with the disease
- Although vancomycin impregnated bone cement spacer (VIBCS) have been used to reduce the risk of PJI in revision arthroplasty, a newer strategy of intrawound (IW) vancomycin powder placement has recently gained attention
- Vancomycin has a high propensity for causing nephrotoxicity and the optimal IW vancomycin dose has not been described
- The purpose of this study was to report real-world safety data in patients receiving IW vancomycin with a concomitant VIBCS for hip, knee, and shoulder revision arthroplasties

METHODS

- This was a single-center, retrospective chart review of adult patients undergoing revision hip (THA), knee (TKA), or shoulder (SA) arthroplasty with a VIBCS between April 2016 and October 2019
- Patients receiving IW vancomycin without placement of a VIBCS were excluded
- Baseline characteristics and clinical outcomes of patients who received IW vancomycin powder placed into and around the joint with a VIBCS were compared to patients who received a VIBCS alone (usual care)
- All procedures were performed by one of three orthopedic surgeons
- The primary endpoint was the development of vancomycin induced nephrotoxicity (VIN) within 10 days post-operatively while post-operative length of stay was a secondary endpoint
- VIN was defined as a serum creatinine greater than 1.5 times the patient's baseline serum creatinine in the presence of a serum vancomycin level > 20 mg/L
- Per the institution's protocol, all patients receiving vancomycin with the development of new onset renal injury had a serum vancomycin level ordered
- Estimated glomerular filtration rate was performed using Cockcroft-Gault with adjusted body weight and staging of chronic kidney disease (CKD) was done in accordance with KDIGO guidelines

RESULTS

Analysis

- Of the 29 patients screened, 5 patients were excluded for receipt of IW vancomycin without placement of a VIBCS.
- Of the 24 patients included, 14 patients received IW vancomycin at a median dose (Range) of 5g (4-10)
- The 6 patients who experienced VIN had a median (IQR) serum vancomycin random level of 35 mg/L (27.6-44.3) at a median post-operative time (IQR) to nephrotoxicity of 1.5 days (1-2)

Baseline characteristics and clinical outcomes	IW Vancomycin (n=14)	Usual Care (n= 10)	P- Value
Age, median (IQR)	59 (54.3-67.8)	68 (65.5-78.8)	0.065[1]
Female sex, n (%)	4 (28.6)	5 (50)	0.403[2]
Stage IIIa CKD or worse, n (%)	2 (14.3)	5 (50)	0.085[2]
Adjusted body weight, median (IQR)	90.3 (71.9-94.2)	69.6 (59.4-87.9)	0.053[1]
Baseline Serum creatinine, median (IQR)	0.9 (0.8-1)	1 (0.9-1.2)	0.143[1]
≥ 72 hours of IV vancomycin, n (%)	5 (35.7)	3 (30)	1.000[2]
IV Contrast during admission, n (%)	1 (7.1)	2 (20)	0.554[2]
≥ 24 hours of Ketorolac, n (%)	9 (64.3)	7 (70)	>0.999[2]
Post-operative hypotension, n (%)	8 (57.1)	4 (40)	0.408[2]
Aminoglycoside powder placement, n (%)	3 (21.4)	0 (0)	0.239[2]
Vancomycin dose per 40g of polymethyl methacrylate, median (IQR)	5 (4-5)	5 (4.1-5)	>0.999[1]
Aminoglycoside dose per 40g of polymethyl methacrylate, median (IQR)	n=9 2.4 (2.4-2.4)	n=7 2.4 (2.4-2.4)	>0.999[1]
Procedure, n (%)			>0.999[2]
2-Stage TKA	9 (64.3)	6 (60)	
2-Stage THA	4 (28.6)	3 (30)	
Other[#]	1 (7.1)	1 (10)	
Pathogen, n (%)			0.749[2]
***Staphylococcus* aureus**	7 (50)	2 (20)	
Coagulase-negative staphylococci	2 (14.3)	2 (20)	
***Enterococcus* spp./ VGS**	1 (7.1)	2 (20)	
Group B *Streptococcus*	1 (7.1)	1 (10)	
Culture negative	1 (7.1)	1 (10)	
Other[%]	2 (14.3)	2 (20)	
Vancomycin induced nephrotoxicity, n (%)	6 (42.9)	0 (0)	**0.02**[2]
Post-surgery length of stay, median (IQR)	4.5 (3-7.3)	4 (3.3-5)	0.72[1]

[1]Mann Whitney *U* [2]Fisher's Exact Test
[#]Permanent resection arthroplasty: 2-stage shoulder arthroplasty: 1 patient; 1-stage THA: 1 patient
[%]*P. fluorescens*: 1 patient; *E. aerogenes*: 1 patient; *C. striatum*: 1 patient; *P. micra*; 1 patient

Patients requiring dialysis catheter placement

- Two patients required dialysis catheter placement as a consequence of VIN

- Patient 1:
  - 88-year-old female with a history of bilateral THA placed 9 years prior to presentation was managed for *Staphylococcus aureus* THA infection
  - Underwent a right THA single-stage revision
  - 1 pack of SmartSet MV® bone cement was mixed with 5 g of vancomycin and 2.4 g of tobramycin and half was used to make the Prostalac® stem while the other half was then pressurized into the acetabulum and the Prostalac® acetabular component
  - Prior to closure, 5 g of vancomycin powder was also applied to the hip joint itself and an additional 5 g of vancomycin powder and 2.4 g of tobramycin was then applied into the abductors as well as anterior and posterior aspect of the hip outside of the capsule
  - Two days following surgery, the patient became anuric and required emergent dialysis
    - Vancomycin and tobramycin levels at that time were found to be 71.6 mg/L and 35.9 mg/L, respectively, despite not receiving systemic vancomycin or tobramycin

- Patient 2:
  - 53-year-old male who underwent a right TKA replacement a decade prior to presentation was managed for culture negative TKA infection
  - During the initial stage of a two-staged procedure 2.5 packs of SmartSet MV® bone cement powder was mixed with 3 vials of monomer, 10 g of vancomycin and 4.8 g of tobramycin was used to make the KASM® size large femur and tibial mold
  - An additional 2.5 packs of SmartSet MV® with 3 vials of monomer, 10 g of vancomycin and 4.8 g of tobramycin was molded and loosely cemented into place using cement dowels down the intramedullary space with excess cement excised.
  - Prior to closure, 5g of vancomycin powder was also applied throughout the entire inner aspect of the knee.
  - Two days following the procedure the patient developed oliguria, his creatinine increased to 8.21 mg/dL from his baseline of 0.9 mg/dL and he developed severe metabolic acidosis requiring dialysis catheter placement
  - Despite not receiving systemic vancomycin, the patient was found to have a serum vancomycin level of 46.7 mg/L

CONCLUSIONS

- Our experience with IW vancomycin at a median dose of 5g in combination with VIBCS was associated with an increased risk of nephrotoxicity in our patients
- Therefore, re-evaluation of the use of IW vancomycin at these doses is warranted