Impact of Vancomycin-Loaded Bone Cement on Systemic Vancomycin Exposure and the Risk of Acute Kidney Injury in Periprosthetic Joint Infection

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Introduction

Vancomycin-loaded bone cement (VLBC) is frequently employed during the first stage of two-stage exchange arthroplasty for periprosthetic joint infection (PJI) to achieve high local antibiotic concentrations. While local delivery is beneficial, concerns regarding systemic absorption and potential nephrotoxicity persist. This study aimed to evaluate the incidence of acute kidney injury (AKI) and the impact of VLBC on systemic vancomycin exposure in patients with PJI.

Patients and methods

We conducted a retrospective cohort study of 317 patients with hip or knee PJI (excluding end-stage renal disease). The VLBC group (n = 236) consisted of patients undergoing two-stage exchange arthroplasty. The non-VLBC group (n = 81) comprised patients undergoing debridement, antibiotics, and implant retention (DAIR) (80.7%) or one-stage exchange arthroplasty (13.3%). The primary outcome was AKI, defined by the Kidney Disease: Improving Global Outcomes (KDIGO) criteria (serum creatinine increase ≥0.3 mg/dL within 48h or ≥1.5 times baseline). To isolate local elution effects, ΔAUC_{ss} (difference between observed and predicted area under the curve at steady state) and $\Delta Trough_{ss}$ were calculated using a population pharmacokinetic model, adjusting for intravenous (IV) vancomycin dose and renal function.

Table 1. Baseline patient characteristics

Variable	Non-VLBC (n = 81)	VLBC (n = 236)	P value
Patient characteristics			
Age, years	69 (59 –75)	67 (60 –73)	0.38
Male sex	31 (38.3)	104 (44.1)	0.44
Body mass index, kg/m²	25 (23–28)	24 (21–27)	0.02
Diabetes mellitus	23 (28.4)	78 (33)	0.52
Joint			
Hip	41 (50.6)	153 (64.8)	0.03
Knee	40 (49.4)	83 (35.2)	
Relapsed cases	13 (16.2)	45 (19.1)	0.69
Presence of sinus tract	11 (16.7)	39 (17.5)	>0.99
Laboratory findings			
WBC, /mm³	7930 (6390 –10170)	7545 (6195 –9085)	0.13
ESR, mm/h	76 (42 –108)	76 (47 –101)	0.80
CRP, mg/dL	5.4 (1.4–15.1)	2.7 (1.1 –6.4)	0.009
Serum creatinine, mg/dL	0.7 (0.6 –0.9)	0.7 (0.6–0.9)	0.66
Causative pathogens			
Methicillin-susceptible *S. aureus*	14 (17.3)	23 (9.7)	0.11
Methicillin-resistant *S. aureus*	4 (4.9)	24 (10.2)	0.23
Coagulase-negative staphylococci	18 (22.2)	47 (19.9)	0.78
Gram-negative bacteria	11 (13.6)	22 (9.3)	0.38
Streptococcus species	12 (14.8)	13 (5.5)	0.02
Enterococcus species	1 (1.2)	9 (3.8)	0.46
Candida species	3 (3.7)	5 (2.1)	0.42
Polymicrobial	1 (1.2)	4 (1.7)	>0.99
Unknown	12 (14.8)	76 (32.2)	0.004
Acute kidney injury	12 (14.8)	29 (12.3)	0.69

Note. Data are presented as No. (%) of patients or median (interquartile range) unless otherwise indicated.

Results

The non-VLBC group exhibited clinical features consistent with acute hematogenous PJI, characterized by significantly higher median C-reactive protein levels (5.4 vs. 2.7 mg/dL; P = 0.009) and a greater prevalence of *Streptococcus* species (14.8% vs. 5.5%; P = 0.02). The overall incidence of AKI did not differ significantly between the VLBC and non-VLBC groups (12.3% vs. 14.8%; P = 0.69) (Table 1). In multivariate logistic regression analysis, glomerular filtration rate (aOR 0.97; 95% CI, 0.94–0.99) was identified as an independent risk factor for AKI. Among 125 patients receiving IV vancomycin, the high-dose VLBC group (≥4g/40g bone cement) showed significantly higher systemic exposure compared to the IV-only group (ΔAUC_{ss}: median 51.2 vs. –24.4 mg·h/L, $P < 0.001$; $\Delta Trough_{ss}$: median 1.5 vs. –1.4 mg/L, $P < 0.001$) (Table 2). Notably, the proportion of patients with supra-therapeutic exposure (AUC >600 mg·h/L) was substantially higher in the high-dose VLBC group (39.1%) compared to the IV-only (25.0%) and low-dose VLBC (19.0%) groups. Figure 1 presents a comparison of the $\Delta Trough_{ss}$ among three groups, normalized to 0 relative to the control median. Observed-predicted plots between 3 groups were shown in Figure 1B.

Figure 1. Effect of VLBC on systemic vancomycin exposure

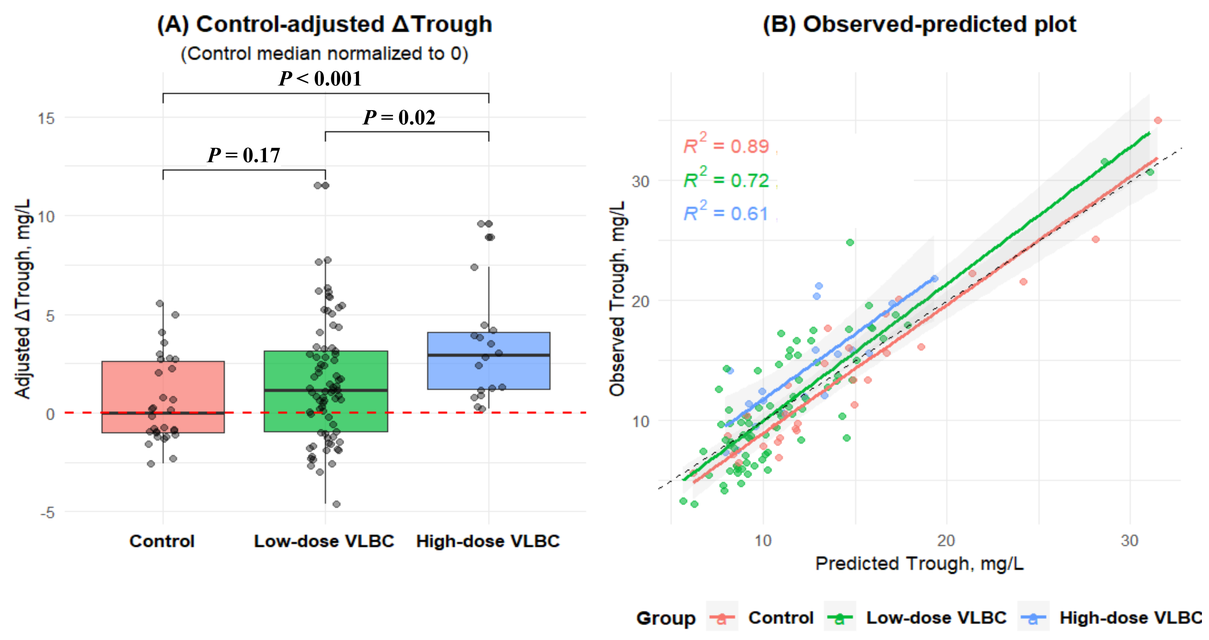

Table 2. Pharmacokinetic parameters

Variable	Control (IV only) (n = 30)	Low-dose VLBC (n = 77)	High-dose VLBC (n = 18)
Vancomycin dose			
IV vancomycin (mg/kg/day)	30.0 (28.8–31.2)	29.9 (28.6–30.4)	30.0 (29.4–30.4)
Vancomycin in cement (g/batch)	NA	2.0 (1.7–2.0)	4.0 (4.0–5.0)
Pharmacokinetic parameters			
Observed $Trough_{ss}$ (mg/L)	10.9 (8.5–16.1)	10.3 (7.4–14.6)[a]	14.5 (11.3–15.8)[b]
Observed AUC_{ss} (mg·h/L)	471 (410–611)	459 (368–570)[a]	522 (484–631)[b]
$\Delta Trough_{ss}$ (mg/L)	-1.4 (−2.4, 1.3)	-0.3 (-2.4, 1.7)	1.5 (-0.3, 2.8)
ΔAUC_{ss} (mg·h/L)	−24.4 (−50.5, 47.8)	8.6 (-30.3, 58.5)	51.2 (5.9–54.3)[b]

Note. Data are presented as median (interquartile range) unless otherwise indicated.

[a] No significant difference ($p > 0.05$) between the non-VLBC(IV-only) and low-dose VLBC groups.

[b] $p < 0.001$ for the comparison between non-VLBC(IV-only) and high-dose VLBC groups

Conclusion

While VLBC use was not associated with an increased risk of AKI, high-dose applications (≥4g/40g) significantly elevated systemic exposure, with nearly 40% of these patients reaching supra-therapeutic levels. Given that conventional dosing may underestimate the total vancomycin burden in this subgroup, risk-stratified therapeutic drug monitoring (TDM) is essential to prevent potential dose-related toxicity and optimize patient safety.