

Day-one local fluid and serum antibiotic concentrations after vancomycin-gentamicin PMMA coating of tibial intramedullary nails: an observational series

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Abstract

Background: Antibiotic-loaded polymethylmethacrylate (PMMA) coatings provide a means of delivering antimicrobials near intramedullary implants. Human data relating the gentamicin quantity incorporated into the coating to local fluid and serum concentrations remain limited.

Methods: Thirty patients with vancomycin (2 g)-containing PMMA-coated tibial nails were evaluated according to incorporated gentamicin dose: 0.5 g (n=9), 1 g (n=14), or 2 g (n=7). Patient-level day-one fluid and serum antibiotic measurements, concomitant systemic antibiotics, recorded adverse events, and deep infection at six months were assessed. Group comparisons used Kruskal–Wallis tests; dose associations were assessed using Spearman correlation. The analysis was exploratory.

Results: Mean (SD) local fluid concentrations were 1172.7 (138.3) mg/L for vancomycin and 434.8 (241.0) mg/L for gentamicin. Gentamicin concentrations were 202.0 (22.5), 388.1 (57.0), and 827.2 (83.9) mg/L across increasing PMMA gentamicin doses (Kruskal–Wallis $P < 0.001$; Spearman $\rho = 0.927$). With vancomycin loading fixed, local vancomycin concentrations decreased across the same groups ($\rho = -0.475$; $P = 0.008$). Mean serum measurements were 1.80 (0.35) $\mu\text{g/mL}$ for vancomycin and 0.60 (0.15) $\mu\text{g/mL}$ for gentamicin. Thirteen patients also received systemic gentamicin. Deep infection was recorded in two patients (2/30; 6.7%), both in the 0.5-g group (2/9 vs 0/21; Fisher $P = 0.083$). One patient had recorded acute kidney injury; no ototoxicity or local allergic reaction was recorded.

Conclusions: Greater gentamicin loading was strongly associated with higher day-one local gentamicin concentrations, without an observed serum dose gradient. Local and serum measurements differed substantially. These findings describe early measured concentrations but do not establish sustained elution, comparative infection prevention, or absence of systemic toxicity.

Keywords: antibiotic-loaded bone cement; gentamicin; intramedullary nail; local drug delivery; polymethylmethacrylate; tibial fracture; vancomycin

Introduction

Infection associated with fracture fixation is clinically consequential because bacterial persistence, impaired soft-tissue condition, and failure of bone union may coexist. Consensus recommendations distinguish confirmatory from suggestive features of fracture-related infection (FRI) and emphasize appropriate tissue sampling, adequate debridement, stability, and soft-tissue management. A diagnosis of deep infection therefore requires more than a change in serum inflammatory markers or an antibiotic concentration above a laboratory reference value. [1,2,3]

Intramedullary antibiotic delivery has long been explored as an adjunct to surgery for infected nonunion and osteomyelitis. Early antibiotic cement rods demonstrated the feasibility of filling the medullary canal with an antibiotic carrier; subsequent interlocking nail techniques combined local delivery with fixation. Prospective experience with commercially gentamicin-coated titanium nails provides additional clinical context, although that coating system differs fundamentally from a PMMA mantle prepared with two antibiotics. [4,5,6]

PMMA can contain heat-stable antibiotics and release a portion into nearby fluid after implantation. Its appeal is high exposure close to the operative field with a potentially lower circulating concentration than would accompany an equivalent systemic dose. Yet elution varies with cement composition, porosity, mixing technique, implant geometry, antibiotic quantity, and the surrounding fluid environment. Local antibiotic placement remains an adjunct to, rather than a substitute for, careful surgical care and appropriate systemic therapy. [7,8,9]

Dual-agent cement warrants particular attention. In-vitro experiments show that antibiotic combinations may change the elution of either constituent, but the direction and magnitude depend on the combination and cement formulation. Penner and colleagues described enhanced elution when vancomycin and tobramycin were combined, whereas work with vancomycin and gentamicin demonstrated distinct release profiles. Broader assessments

likewise caution against extrapolating a single mixture or in-vitro result to every PMMA device. [10,11,12]

A further distinction concerns microbiological interpretation. Planktonic susceptibility breakpoints classify bacterial isolates under defined testing and exposure conditions; they are not validated measures of antibiotic activity against an established implant-associated biofilm. Differences in pathogen susceptibility, depth of tissue penetration, and release over time may therefore separate a high initial fluid reading from the clinical course. [13]

Although larger series have reported outcomes after antibiotic-coated intramedullary nails, the relationship between antibiotic loading, patient-level early fluid concentration, systemic detection, and subsequent events remains incompletely described. [14] The present analysis evaluates these relationships in 30 patients with PMMA-coated tibial nails containing fixed-dose vancomycin and three gentamicin dose levels. The primary pharmacological focus is the day-one local gentamicin concentration across coating doses; serum measurements, local vancomycin variation, and six-month events are descriptive or exploratory secondary observations.

Methods

Study design and available observations

This observational case series comprised 30 patients treated with a PMMA-coated tibial intramedullary nail. All 30 patient-level entries were included in the analysis; there were no missing entries in the 14 available data fields. No untreated or alternative-coating comparator group was available. The study was conducted at Vinayaka Mission's Kirupananda Variyar Medical College & Hospital, Salem, after approval from the Institutional Ethics Committee (IEC No. VMK VMC&11/IEC/25/215). The report follows the principles of transparent observational reporting. [15]

The patient-level variables were nail-coating antibiotic doses, day-one local fluid and serum concentrations of both antibiotics, systemic

antibiotic agent and course duration, recorded acute kidney injury (AKI), ototoxicity, local allergic reaction, deep infection at six months, and subsequent antibiotic treatment duration. Age, sex, fracture type, baseline renal function, baseline infection status, microbiological results, and operative characteristics were not provided. Consequently, clinical confounding cannot be adequately adjusted for.

Local antibiotic loading and concomitant antimicrobial therapy

Every PMMA coating contained 2 g of vancomycin. Gentamicin loading was 0.5 g in nine patients, 1 g in 14, and 2 g in seven. The PMMA powder mass, brand, mixing procedure, polymerization technique, nail dimensions, coated surface area, and selection criteria for gentamicin dose were not specified. Systemic regimens were cefazolin alone, cefazolin with gentamicin, or piperacillin–tazobactam. Durations were three, five, or seven days (Table 1).

Table 1. Local and systemic antibiotic treatment in the 30-patient series

Treatment characteristic	n	%
Vancomycin in PMMA: 2 g	30	100.0
Gentamicin in PMMA: 0.5 g	9	30.0
Gentamicin in PMMA: 1 g	14	46.7
Gentamicin in PMMA: 2 g	7	23.3
Systemic cefazolin	13	43.3
Systemic cefazolin + gentamicin	13	43.3
Systemic piperacillin–tazobactam	4	13.3

Systemic courses were three days in 16 patients (53.3%), five days in seven (23.3%), and seven days in seven (23.3%); mean (SD) duration was 4.4 (1.7) days. PMMA, polymethylmethacrylate.

Antibiotic measurements and endpoints

For each patient, one concentration for each antibiotic was available in local fluid and one in serum, all designated as day-one values. The serum measurements were designated as “peak” values; however, the precise collection times, laboratory assay, sample matrix or anatomical fluid source, and pharmacokinetic sampling scheme were not supplied. Serum values are therefore treated as recorded day-one concentrations rather than validated maximum concentrations (C_{max}). Local fluid concentrations were expressed in mg/L and

serum concentrations in $\mu\text{g/mL}$. These units are numerically equivalent ($1 \mu\text{g/mL} = 1 \text{ mg/L}$). For each patient, a fluid-to-serum concentration ratio was calculated from the paired day-one values. The ratio describes the difference between sampling compartments at the available time points; it is not an estimate of total release, penetration, or systemic exposure.

Local concentrations were additionally divided by an illustrative 2 mg/L value. Although 2 mg/L may coincide with selected organism–antibiotic interpretive thresholds, EUCAST tables are organism-specific and exposure-dependent; this numerical comparison was not used to infer isolate susceptibility, biofilm eradication, or clinical efficacy. [16]

Systemic vancomycin guidance for serious methicillin-resistant *Staphylococcus aureus* infection uses an AUC₂₄/MIC framework and cannot be applied to these isolated serum samples. Neither an AUC₂₄ nor the cumulative systemic dose absorbed from the coating could be estimated. [17]

The adverse-event variables were binary entries for AKI, ototoxicity and local allergy. Baseline and repeat creatinine concentrations, audiometry and the specific criteria used for these diagnoses were unavailable. The six-month outcome was the documented presence or absence of “deep infection”; confirmatory diagnostic findings and causative pathogens were unavailable. These endpoints are reported as recorded, without independent adjudication.

Systemic antibiotic exposure and causal attribution

Thirteen patients were treated with systemic gentamicin in addition to the gentamicin-containing PMMA. Accordingly, serum gentamicin may have arisen from one or both routes, and the available data cannot separate the two contributions. Related clinical studies have demonstrated measurable systemic antibiotic concentrations after implantation of antibiotic-loaded cement devices, underscoring the need for serial measurements and accurate concomitant medication information. [18]

Because aminoglycosides and vancomycin can contribute to renal injury under some circumstances, an early low concentration

cannot establish the absence of nephrotoxicity, especially without serial kidney-function measurements. [19] Consistent with FRI consensus recommendations, systemic therapy and surgery should be considered alongside local drug delivery when interpreting subsequent infection events. [20]

Statistical methods

Continuous variables are summarized as mean (sample standard deviation), median, interquartile range (IQR) and observed range as appropriate. Kruskal–Wallis tests compared the three loading groups. Spearman rank correlation (ρ) assessed monotonic relationships involving gentamicin dose; correlation of local and serum concentrations was also examined. The six-month deep-infection flag was compared between the 0.5-g group and the combined 1- and 2-g groups using a two-sided Fisher exact test. Wilson score 95% confidence intervals (CIs) describe event proportions. All analyses used the 30 observations without imputation. Tests were two-sided, with $P < 0.05$ treated as an exploratory threshold; no correction was applied for multiple comparisons. No multivariable outcome model was attempted because only two deep-infection events occurred.

Results

Cohort treatment characteristics

Gentamicin loading was 0.5, 1, and 2 g in nine, 14, and seven patients, respectively. Twenty-six patients received a cefazolin-containing systemic regimen, of whom 13 also received gentamicin; four received piperacillin–tazobactam. Systemic gentamicin use differed descriptively across coating-dose groups: 4 of 9 at 0.5 g, 8 of 14 at 1 g, and 1 of 7 at 2 g. The clinical indication for regimen selection and the timing of blood sampling relative to systemic administration were unavailable.

Day-one concentrations in local fluid and serum

The mean (SD) day-one local fluid vancomycin concentration was 1172.7 (138.3) mg/L, with a median of 1169.5 mg/L and a range of 906.0–1477.8 mg/L. Local gentamicin averaged 434.8 (241.0) mg/L, with a median of 381.6 mg/L and a range of 172.3–935.6 mg/L. Mean serum concentrations were 1.80 (0.35) $\mu\text{g/mL}$ for vancomycin and 0.60 (0.15) $\mu\text{g/mL}$ for gentamicin. All recorded gentamicin serum values were below 1 $\mu\text{g/mL}$, and five vancomycin values exceeded 2 $\mu\text{g/mL}$ (Table 2).

Table 2. Descriptive distribution of day-one measured antibiotic concentrations (n = 30)

Measurement	Mean (SD)	Median [IQR]	Range
Local vancomycin (mg/L)	1172.7 (138.3)	1169.5 [1093.6–1255.2]	906.0–1477.8
Local gentamicin (mg/L)	434.8 (241.0)	381.6 [237.3–470.9]	172.3–935.6
Serum vancomycin ($\mu\text{g/mL}$)	1.80 (0.35)	1.80 [1.65–1.92]	1.03–2.79
Serum gentamicin ($\mu\text{g/mL}$)	0.60 (0.15)	0.61 [0.46–0.72]	0.36–0.93
Local:serum vancomycin ratio	677.2 (166.3)	654.8 [565.4–745.6]	443.5–1212.2
Local:serum gentamicin ratio	752.9 (429.2)	624.8 [539.1–889.4]	212.7–1831.2

IQR, interquartile range; SD, standard deviation. Local/serum ratios were calculated for each paired patient observation before summarization. No concentration–time curves were available.

Concentrations according to gentamicin loading

Day-one local gentamicin concentrations increased in an ordered pattern across the loading groups, with means (SD) of 202.0 (22.5), 388.1 (57.0) and 827.2 (83.9) mg/L for 0.5, 1 and 2 g, respectively. The three observed ranges did not overlap (172.3–238.5; 269.0–478.2; and 680.4–935.6 mg/L). The Kruskal–Wallis statistic was $H=24.93$ ($P=3.86 \times 10^{-6}$), and Spearman ρ was 0.927 ($P=1.85 \times 10^{-13}$), confirming a strong within-sample monotonic association (Table 3; Figure 1).

Although the amount of vancomycin incorporated into every coating was fixed at 2 g, its local fluid concentration was lower in groups with more gentamicin (mean 1261.1, 1168.4 and 1067.6 mg/L; Kruskal–Wallis $H=6.62$, $P=0.0365$; Spearman $\rho=-0.475$, $P=0.00794$). This observation does not

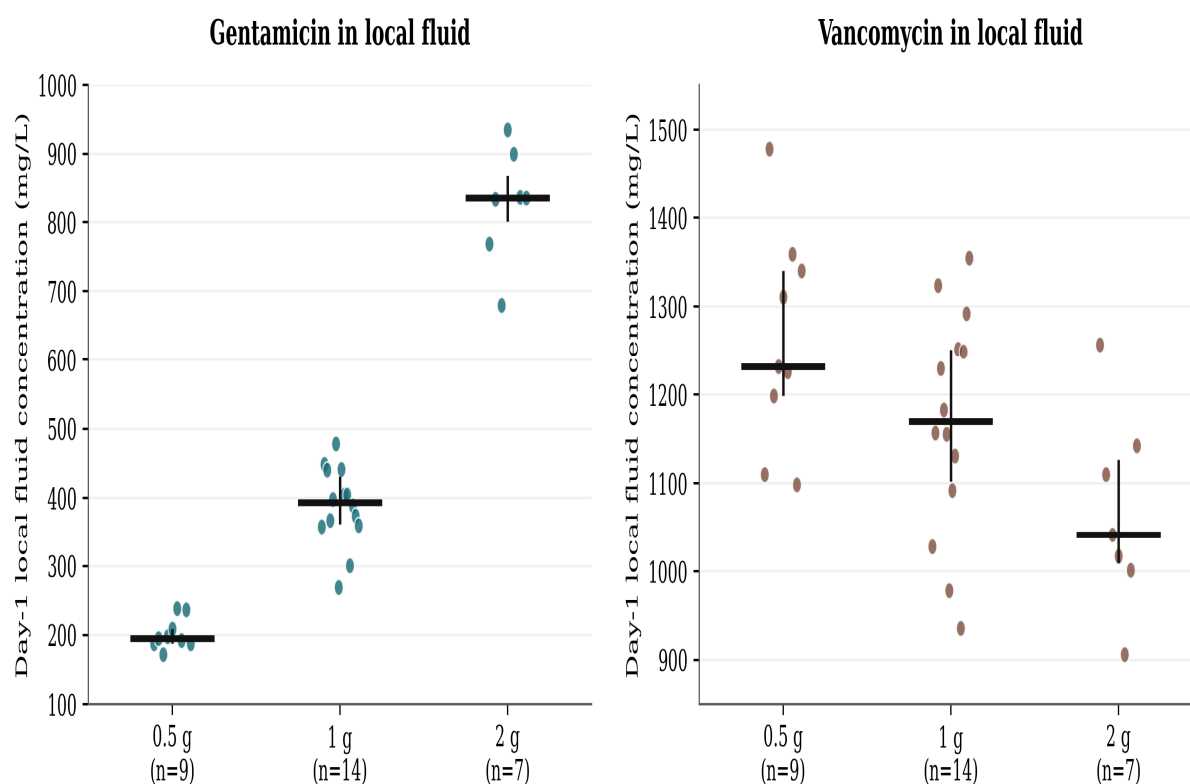
establish a direct inhibitory effect of gentamicin on vancomycin release; unmeasured coating and sampling characteristics could also explain the association.

There was no detectable difference in the recorded serum measurements across loading groups (vancomycin $P=0.753$; gentamicin $P=0.744$). Dose–serum rank associations were small (vancomycin $\rho=-0.089$, $P=0.638$; gentamicin $\rho=0.137$, $P=0.472$). Paired fluid–serum rank correlations were similarly weak (vancomycin $\rho=0.067$, $P=0.727$; gentamicin $\rho=0.205$, $P=0.278$). These nonsignificant findings not be interpreted as evidence that systemic absorption is dose-independent.

Table 3. Day-one concentrations by gentamicin quantity in the PMMA coating

Outcome	0.5g (n=9)	1g (n=14)	2g (n=7)	Kruskal–Wallis P
Local vancomycin (mg/L)	1261.1 (122.8)	1168.4 (126.8)	1067.6 (113.2)	0.0365
Local gentamicin (mg/L)	202.0 (22.5)	388.1 (57.0)	827.2 (83.9)	<0.001
Serum vancomycin ($\mu\text{g/mL}$)	1.77 (0.28)	1.87 (0.43)	1.70 (0.25)	0.753
Serum gentamicin ($\mu\text{g/mL}$)	0.56 (0.16)	0.60 (0.12)	0.63 (0.21)	0.744
Concurrent systemic gentamicin, n	4	8	1	—

Values are mean (SD), except concurrent systemic gentamicin (count). P values are exploratory and unadjusted for multiplicity. The PMMA vancomycin dose was 2 g in all groups.



Gentamicin loading per PMMA-coated nail | Points: individual patients; black bars: median and interquartile range

Figure 1. Day-one local fluid vancomycin and gentamicin concentrations by incorporated gentamicin dose. Each point represents a patient; horizontal black bars mark the median and vertical marks the interquartile range. Vancomycin loading was identical across groups (2 g).

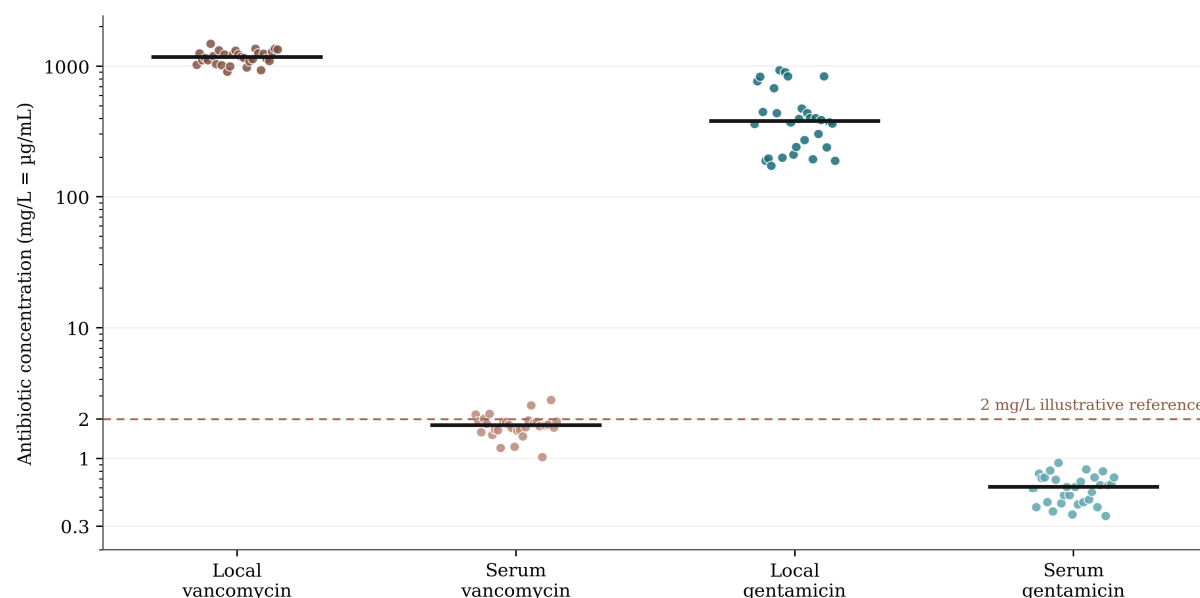


Figure 2. Individual day-one measurements in local fluid and serum, shown on a logarithmic concentration axis. Because 1 $\mu\text{g/mL}$ equals 1 mg/L , both sampling compartments can be plotted on one numeric scale. The dashed line denotes an illustrative 2 mg/L reference, not a universal pharmacodynamic threshold. Horizontal black bars indicate medians.

Local-to-serum relationships and illustrative benchmark

Median patient-level local-to-serum ratios (Figure 2) were 654.8 for vancomycin (range 443.5–1212.2) and 624.8 for gentamicin (range 212.7–1831.2). When divided by the illustrative 2 mg/L value, local vancomycin readings corresponded to 453–739-fold and local gentamicin readings to 86–468-fold. These ratios quantify a contrast between sampled fluids; they do not determine the free active concentration at the bone–implant interface or the pathogen-specific antimicrobial effect.

Recorded infection and adverse events through six months

Deep infection was recorded in two of 30 patients (6.7%; Wilson 95% CI 1.8–21.3%). Both occurred in the 0.5-g gentamicin group (2/9, 22.2%); no deep infection was recorded in the 21 patients receiving 1 or 2 g (0/21). The difference was not statistically significant in a two-sided Fisher exact test ($P=0.0828$). The event count was too small to estimate a reliable dose effect or exclude important baseline imbalances (Table 4).

One of 30 patients had recorded AKI (3.3%; Wilson 95% CI 0.6–16.7%). This patient received 2 g of gentamicin in the PMMA

coating and a three-day course of systemic cefazolin. The day-one measured serum concentrations were 0.39 $\mu\text{g/mL}$ for gentamicin and 1.67 $\mu\text{g/mL}$ for vancomycin. There were no recorded cases of ototoxicity or local allergic reaction; for either outcome, the upper Wilson 95% confidence limit with zero events in 30 patients is 11.4%.

Table 4. Six-month infection and recorded adverse events by PMMA gentamicin loading

Recorded event	0.5 g (n=9)	1 g (n=14)	2 g (n=7)	Overall (n=30)
Deep infection by six months	2	0	0	2 (6.7%)
Six-week additional antibiotic course	2	0	0	2 (6.7%)
Acute kidney injury	0	0	1	1 (3.3%)
Ototoxicity	0	0	0	0
Local allergic reaction	0	0	0	0

The deep-infection comparison was 2/9 versus 0/21 (two-sided Fisher exact $P=0.0828$). Binary events were not accompanied by diagnostic adjudication or laboratory confirmation in the study dataset.

The two deep-infection cases both had gentamicin loading of 0.5 g and received cefazolin without systemic gentamicin. Their local day-one gentamicin readings were 192.5 and 187.5 mg/L; local vancomycin readings were 1358.6 and 1339.7 mg/L. Each subsequently received a six-week additional antibiotic course. Individual case details are displayed in Table 5.

Table 5. Day-one observations and treatment in the two patients with recorded deep infection

Patient-level variable	PT-022	PT-030
Gentamicin / vancomycin in PMMA	0.5 g / 2 g	0.5 g / 2 g
Local gentamicin (mg/L)	192.5	187.5
Local vancomycin (mg/L)	1358.6	1339.7
Serum gentamicin (µg/mL)	0.55	0.72
Serum vancomycin (µg/mL)	1.87	1.92
Concomitant systemic antibiotic	Cefazolin	Cefazolin
Systemic course (days)	7	3
Additional course after deep infection	6 weeks	6 weeks

Discussion

In this series of 30 patients, day-one local fluid gentamicin concentrations increased in a dose-dependent pattern: concentrations averaged nearly two-fold higher with 1 g and over four-fold higher with 2 g relative to the 0.5-g dose. Conversely, serum gentamicin concentrations remained low across all cohorts without a demonstrable dose gradient. While these findings document a relationship between incorporated dose and immediate peri-implant fluid levels, they reflect single-point measurements rather than complete systemic pharmacokinetic profiles.

The unusually large difference between local and serum measurements is consistent with the intended compartmental distribution of locally applied antibiotics. Nevertheless, it is important to distinguish concentration at a sampled fluid site from the amount liberated from PMMA. Cement composition, porosity, surface area, preparation method, and local fluid turnover determine how much antibiotic is recovered at any particular time. Studies comparing acrylic cement formulations confirm that elution

profiles differ even when nominal drug loading is similar. [21]

Despite a uniform 2-g vancomycin load across all implants, measured local vancomycin concentrations declined as the incorporated gentamicin dose increased. Prior in vitro evaluations demonstrate that combining antimicrobials in PMMA can alter individual elution kinetics, with release profiles varying by carrier formulation and additive proportions. In the absence of standardized cement masses and sequential sampling, this negative association cannot be definitively ascribed to drug-drug elution interference alone. However, published in-vitro reports show formulation-specific interactions, including enhancement with tobramycin and a different pattern with gentamicin. [10,11] Without a standardized PMMA mass, mixing protocol and serial eluate samples, the present observations do not identify the mechanism behind the negative association. They should not be used to prescribe an optimal antibiotic ratio.

Prior studies of antibiotic cement-coated nails have primarily evaluated infection control and union after treating infected nonunion or complex fracture-related infection. [5,14] Those reports address the combination of fixation, local antibiotic release, debridement and systemic treatment; they do not isolate the causal contribution of a particular first-day fluid concentration. Technical descriptions of antibiotic-coated interlocking nails demonstrate the feasibility of combining mechanical stability with local antimicrobial delivery but also underscore differences in preparation and clinical indication. [22]

The six-month infection frequency was 2/30. Both events occurred after 0.5-g gentamicin loading; neither patient had a low measured local gentamicin concentration in absolute terms. The 2/9 versus 0/21 pattern was based on only two cases and was not statistically significant. In the absence of fracture classification, initial infection burden, soft-tissue status, pathogen identity and treatment indications, it cannot show that 1 or 2 g prevents deep infection more effectively than 0.5 g. Furthermore, the records do not permit

confirmation that the events fulfilled consensus FRI diagnostic criteria. Six months of follow-up also does not exclude later infection recurrence. Interpretation of circulating drug levels is constrained by single-point sampling. Although documented as peak values, exact post-implantation collection times and serial pharmacokinetic curves were unavailable. Furthermore, 13 of the 30 patients received concomitant parenteral gentamicin, confounding the attribution of measured serum levels between local elution and systemic administration, creating direct confounding of source attribution for circulating gentamicin. Comparison of recorded serum values with intravenous treatment targets cannot establish an AUC₂₄, drug clearance, or risk of cumulative exposure from continued PMMA release. Consequently, a numerical fluid-to-serum ratio should be presented as a paired measurement contrast rather than a measure of the therapeutic index.

One recorded episode of AKI occurred despite a low day-one serum gentamicin concentration. This does not establish that the coating caused the event or that gentamicin was uninvolved; renal injury depends on numerous perioperative and medication-related factors that were not captured. Studies of antibiotic-loaded cement spacers in other orthopaedic settings have identified systemic medication exposures and postoperative renal vulnerabilities as relevant to AKI assessment. [23]

Ototoxicity and local allergy were not recorded in 30 patients, but the absence of observed events in a small series provides limited reassurance. In particular, audiometric screening and standardized toxicity definitions were not documented. Prospective assessment should incorporate baseline kidney function, repeated creatinine testing, careful accounting for systemic aminoglycosides, and appropriately timed serum drug measurements.

Although comparing fluid concentrations against an arbitrary 2-mg/L reference illustrates local drug abundance, fold-excess values cannot be equated with clinical efficacy or biofilm eradication. Standard susceptibility breakpoints apply to planktonic bacteria under controlled

conditions, whereas pathogens embedded within mature implant-associated biofilms frequently tolerate antimicrobial concentrations several orders of magnitude above conventional minimum inhibitory concentrations. Biofilm tolerance and local tissue conditions limit the predictive value of a single concentration benchmark. [24]

The two later infections occurred despite local day-one concentrations that exceeded the illustrative comparator by large margins. These paired findings emphasize the distinction between immediate drug recovery and the broader requirements of infection control: surgery, stability, host characteristics, culture-directed treatment and sufficiently long antimicrobial exposure.

Strengths and limitations

Strengths include complete patient-level data for the specified variables, reporting of both antibiotics in local fluid and serum, a fixed vancomycin loading across the three gentamicin groups, and transparent accounting of recorded six-month events. Patient-level measurements permitted verification of the descriptive statistics and main nonparametric comparisons.

Limitations are substantial. This is a small, uncontrolled observational series with nonrandom gentamicin dose assignment and potential confounding by concurrent systemic regimens. Cement mass, coating dimensions, cement brand, preparation methods, assay validation, sampling site and collection times were unspecified. No repeated local or serum samples were available, making elution kinetics, release rate, peak concentration and AUC unmeasurable. Important patient characteristics, infection status at implantation, microbiology and organism-specific MICs were unavailable. Clinical endpoints were binary labels without independent confirmation. The limited number of infections prevents meaningful adjustment for confounders; adverse-event ascertainment was not standardized. Multiple exploratory comparisons also increase the chance of false-positive findings. The population to which the observations generalize cannot be defined

reliably without clinical inclusion criteria and setting information.

Implications for further investigation

Prospective studies should specify a standardized PMMA formulation and coating geometry, document antibiotic loading relative to cement mass, and prespecify the source and timing of local fluid and blood samples. Serial measurements during the first days and weeks, bacterial species identification with MIC testing, and validated biofilm-related assessments would better connect local delivery to antimicrobial activity. Recording baseline renal risk, administered systemic doses, debridement, soft-tissue status and recognized FRI criteria would be necessary before claiming a dose-dependent effect on infection or toxicity. Comparative studies with sufficient follow-up and prespecified outcomes are ultimately needed.

Conclusion

In 30 patients receiving vancomycin–gentamicin PMMA-coated tibial intramedullary nails, higher gentamicin loading was strongly associated with higher day-one local fluid gentamicin concentrations. Recorded day-one serum concentrations were much lower, with no clear difference between loading groups; however, sampling times and concurrent systemic gentamicin limit pharmacokinetic interpretation. Two patients had deep infection by six months, and one had recorded AKI. These data characterize early antibiotic measurements but cannot establish an optimal loading dose, sustained antibacterial activity, comparative clinical effectiveness or systemic safety.

Declarations

Ethics approval and consent: The study was approved by the Institutional Ethics Committee of Vinayaka Mission's Kirupananda Variyar Medical College & Hospital, Salem (IEC No. VMK VMC&11/IEC/25/215).

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Competing interests: The authors declare that they have no competing financial or non-financial interests.

Data availability: The analysis used 30 coded patient-level observations. Access to individual records is subject to institutional permission and applicable confidentiality requirements.

Author contributions: VS: concept, design, data analysis, and manuscript drafting. ME: clinical supervision, data collection, and critical revision. AKC: literature review, statistical review, and manuscript editing. All authors read and approved the final manuscript.

Use of Artificial Intelligence (AI)

No generative artificial intelligence or large language model (LLM) tools were used in the conception, data analysis, or writing of this manuscript. Routine spelling, grammar-checking, and reference-management tools were employed strictly to enhance readability, and the authors assume full responsibility for the integrity and accuracy of the content.

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