



Role of Local Vancomycin in Spinal Infections



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Why is this topic Important

- Vancomycin powder is often used locally during elective spine surgery
- There is a gap in knowledge in the usage of vancomycin with bone graft in infected spines
- Ideally local antibiotic delivery above minimum inhibitory concentration (MIC) over a sustained period with minimal effects to osteoblast and osteocytes desired, avoiding systemic side effects





Vancomycin in spinal infections?

- Excellent activity against gram positive bacteria, especially MRSA and coagulase negative staphylococci
- Can also be used in penicillin allergic patients
- Already commonly used in other musculoskeletal infections e.g. prosthetic joint infections
 - Studies show sustained release of vancomycin in antibiotic impregnated cement above MIC for typical staphylococci over 42 days³
- May not be as suitable in spine infections where fusion is key
 - Concerns of vancomycin adversely affecting bone healing and subsequent fusion due to cytotoxicity to osteoblasts in higher doses⁴

³Kittinger C, Eder-Halbedl M, Kühn KD. Impact of Manual Addition of Vancomycin to Polymethylmethacrylate (PMMA) Cements. Antibiotics (Basel). 2024;13(8):721. Published 2024 Aug 1. doi:10.3390/antibiotics13080721





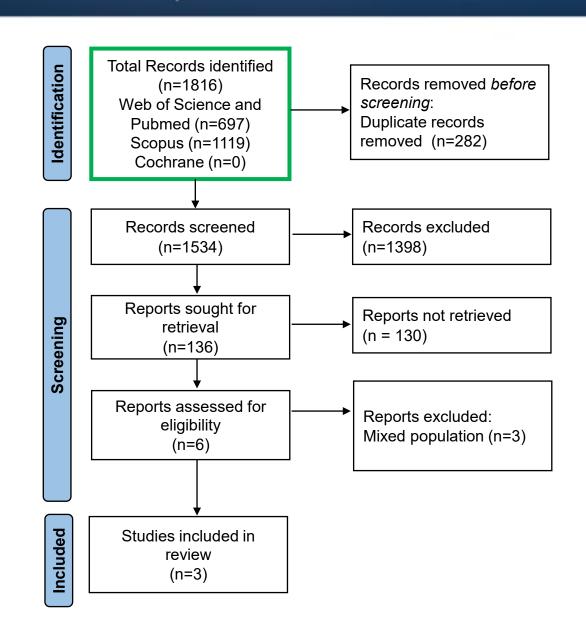
Literature Review/ Process



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Lit Review

- Shiels SM, Raut VP, Patterson PB, Barnes BR, Wenke JC. Antibiotic-loaded bone graft for reduction of surgical site infection in spinal fusion. *Spine J.* 2017;17(12):1917-1925. doi:10.1016/j.spinee.2017.06.039
- Slavnic, Dejan & Tong, Doris & Anton, Gustavo & Bashiti, Rani & Carr, Daniel & Hanson, Connor & Lytle, Evan & Richards, Boyd & Soo, Teck. (2021). Efficacy and Safety with the Use of Antibiotic-impregnated Poly-methyl Methacrylate (Al-PMMA) for Thoracolumbar Spinal Reconstruction in Pyogenic Spondylodiscitis: Retrospective Cohort Study. Interdisciplinary Neurosurgery. 26. 101324. 10.1016/j.inat.2021.101324
- Hanson K, Isder C, Shogren K, et al. The inhibitory effects of vancomycin on rat bone marrow-derived mesenchymal stem cell differentiation. *J Neurosurg Spine*. 2021;34(6):931-935. Published 2021 Apr 2. doi:10.3171/2020.10.SPINE201511



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The Spine Journal 17 (2017) 1917-1925

Basic Science

Antibiotic-loaded bone graft for reduction of surgical site infection in spinal fusion

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Animal study (rabbit)

- Investigating
 - 1. eradication of staphylococcus infection, and
 - capability of spinal fusion with use of vancomycin with demineralized bone matrix (DBM) vs iliac crest bone graft (ICBG)







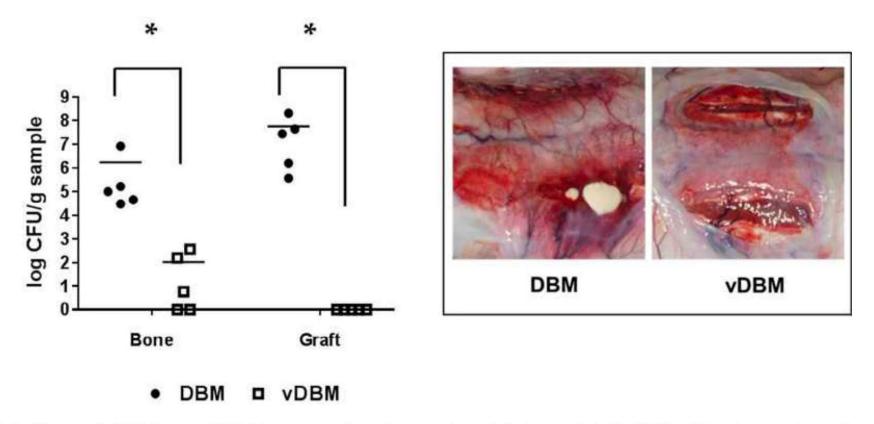
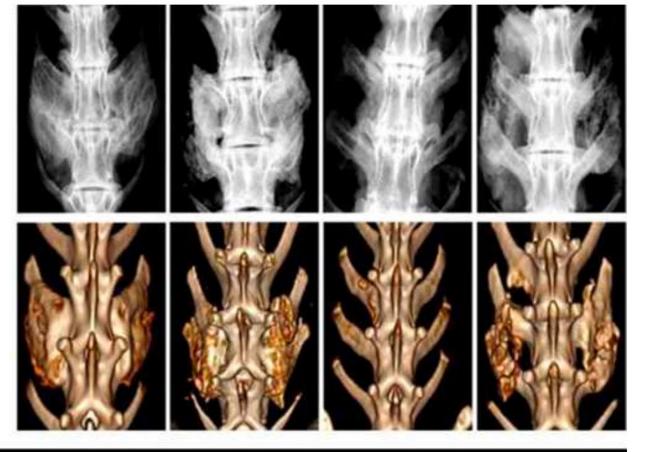


Fig. 2. Antimicrobial efficacy of vDBM versus DBM in a contaminated posterolateral fusion model. (Left) Significantly more bacteria were recovered from the DBM bone and graft than from the vDBM bone and graft (unpaired t test, *, p<.001). (Right) Gross evidence of purulence and devitalized tissue in the DBM groups. vDBM, vancomycin-loaded demineralized bone matrix; DBM, demineralized bone matrix.

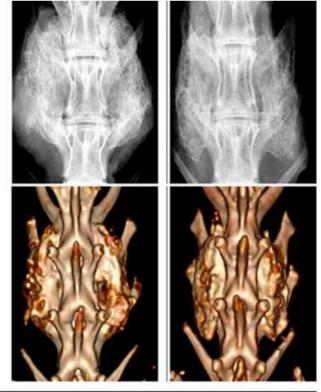




	DBM (-)	VDBM (-)	DBM (+)	vDBM (+)
Manual Palpation	3/3	2/5	4/6	4/6
Plain Radiography	3/3	2/5	1/6*	2/6
3D CT	3/3	2/5	1/6*	2/6





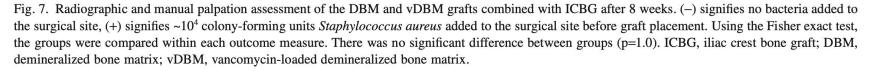


	ICBG + DBM (-)	ICBG + vDBM (+)
Manual Palpation	6/6	6/6
Plain Radiography	6/6	5/6
3D CT	5/6	5/6

Conclusions:
Vancomycin loaded DBM v

Vancomycin loaded DBM was effective in reducing S. Aureus burden

Ineffective as a bone graft alone, But effective as an extender (with ICBG)







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The inhibitory effects of vancomycin on rat bone marrow-derived mesenchymal stem cell differentiation

Kari Hanson,^{1,2} Carly Isder,² Kristen Shogren, MS,² Anthony L. Mikula, MD,¹ Lichun Lu, PhD,^{2,3} Michael J. Yaszemski, MD, PhD,^{2,3} and Benjamin D. Elder, MD, PhD^{1–3}

artments of ¹Neurologic Surgery, ²Orthopedic Surgery, and ³Physiology and Biomedical Engineering, Mayo Clinic, Rochester nesota

- In vitro study of vancomycin on rate bone marrowderived mesenchymal stem cell differentiation
- Vancomycin doses of 0 or 4mg/mL used
- Cells with 0mg/mL vancomycin and no osteogenic factors used as control group
- Cell viability (on day 4 and day 9) and alkaline phosphatase activity used as outcome markers





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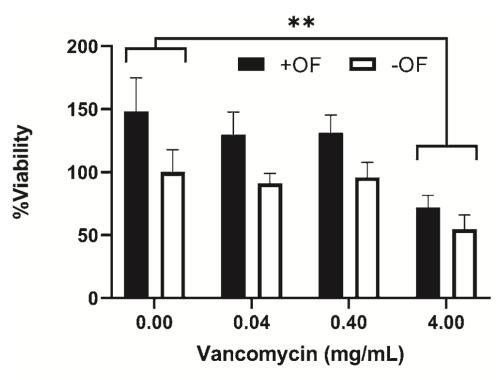


FIG. 1. Cellular viability 4 days after vancomycin treatment. The viability of cells treated with (*black bars*) and without (*white bars*) OFs decreased with increasing concentrations of vancomycin. A 49% decrease in viability was seen between cells treated with 0 and 4 mg/mL vancomycin. **p > 0.0001.

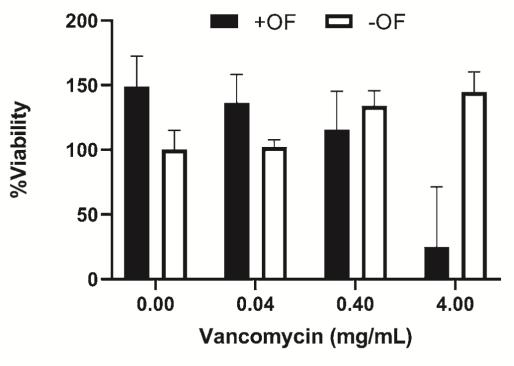


FIG. 2. Cellular viability 9 days after vancomycin treatment. As concentrations of vancomycin increased, there was an observed decrease in viability of cells treated with OFs (*black bars*) and an observed increase in viability of cells not treated with OFs (*white bars*).







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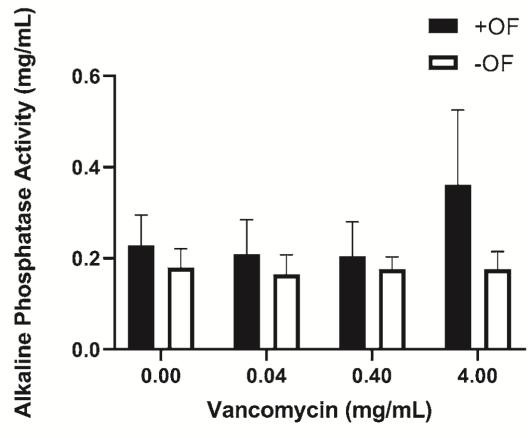


FIG. 4. Alkaline phosphatase activity (mg/mL) at 4 days after vancomycin treatment. Vancomycin had no apparent effects on alkaline phosphatase activity in cells treated with (*black bars*) or without (*white bars*) OFs.

Conclusions:

There is a dose dependent effect on osteogenesis with the use of vancomycin.



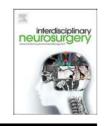


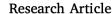


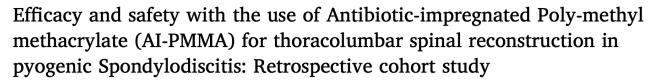
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ABSTRACT

Background: Surgical treatment of spinal osteomyelitis and discitis remains challenging due to the risk of implant colonization. We sought to demonstrate the safety and efficacy of using antibiotic-impregnated poly-methyl methacrylate (AI-PMMA) in spinal reconstruction for pyogenic spondylodiscitis.

Method: We retrospectively analyzed prospective data on consecutive patients who underwent AI-PMMA interbody fusion for thoracolumbar pyogenic spondylodiscitis from December 2011 to October 2016 at a single institution with multiple surgeons. We included consecutive patients who underwent AI-PMMA spinal reconstruction and fusion and were older than 18 years of age. All patients were included in the analysis regardless of their follow-up status who had previous spine surgery in the same area were excluded. Vancomycin powder was mixed with PMMA and tobramycin. The AIPMMA was introduced into the disc space as 5–10 mm beads, then contoured to fit. The primary outcome was fusion using CT or X-ray. Secondary outcomes were recurrent infection, PMMA-related complications, and VAS results. Descriptive statistics and univariate analyses were used. Results: Sixty-two patients were included in the study. The mean follow-up interval was 18.6 months (3–66 months). Sixty-six AI-PMMA levels demonstrated a fusion rate of 100% (95% CI: 94.9%–100%). There was no cement extravasation or embolism. One patient (1.6%) developed a recurrent infection at the same level requiring revision surgery. Five patients (8%) died on long-term follow-up due to non-PMMA/infection-related causes. VAS back showed significant improvement in pain (7.8 vs. 3.5; 95% CI 2.8–5.8; p = 0.00).

Conclusion: We demonstrated that the application of AI-PMMA for spinal reconstruction in pyogenic spondylodiscitis is safe and efficacious. The study is limited by its retrospective design. Prospective studies are warranted.





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Efficacy and safety with the use of Antibiotic-impregnated Poly-methyl methacrylate (AI-PMMA) for thoracolumbar spinal reconstruction in pyogenic Spondylodiscitis: Retrospective cohort study

Dejan Slavnic ^{a,*}, Doris Tong ^{a,*}, Gustavo Anton ^a, Rani Bashiti ^b, Daniel Carr ^a, Connor Hanson ^a, Evan Lytle ^a, Boyd Richards ^a, Teck-Mun Soo ^a

- Minimally invasive approach
- 1g vancomycin and 1g tobramycin used with 40g PMMA mixed to form 5-10mm beads
- Fusion used as primary outcome, assessed on CT and/or x-rays at least 1 year postoperatively
- 62 patients, 66 spinal levels, mean follow up period of 18.6 months
- 40% had MRSA and MSSA infections





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- 1 patient with recurrent infection at the same level (1.6%)
- 5 (8%) patients died of unrelated causes
- No serious surgical complications of cement extravasation/embolism, neurologic or vascular injury, spinal fluid leak or meningitis
- VAS also showed statistically significant improvement in scores for back (preop 7.8 vs postop 3.5, p = 0.00)





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Table 4 Fusion among PMMA levels.

N = 66	N (%)	95% CI
All Levels (N = 66)		
PMMA Levels (n, % fused)	66	94.9–100
	(100)	
More Than One Year Follow-Up ($n = 36$)		
PMMA Levels (n, % fused)	36	90.3–100
	(100)	
Less Than One Year Follow-Up $(n = 30)$		
Fusion confirmed with CT (n, % fused)*	18	81.5–100
	(100)	
Sensitivity Analysis for <1-y Follow-Up w/o CT		
Confirmation $(n = 12)$		
Assuming Fused	66	94.6–100
	(100)	
Assuming Not Fused	54	70.4–90.2
	(81.8)	

Continuous data are presented as mean \pm SD; Categorical data are presented as n (%); p < 0.05 considered significant;

95% CI, 95% confidence interval; PMMA, polymethyl methacrylate;

Conclusion:

Fusion rate of 81.8% across 66 levels when poly-methyl methacrylate (PMMA) beads impregnated with vancomycin and tobramycin was used during surgical intervention



^{*18} patients with less than one-year follow-up obtained CT confirmation.





Question:

What is the role of local vancomycin powder after surgical debridement?

Does the use of antibiotic powder mixed with the bone grafts enable better disease healing?





Response:

Local Vancomycin powder is generally safe and well-tolerated in spinal infections. However, there is literature to support its efficacy.







Agree – 87.9%, Disagree – 3.0%, Abstain – 9.1% (Strong Consensus)





Response:

There is no evidence to show that mixing topical vancomycin powder with bone graft alters healing in patients with infective spondylodiscitis.







Agree – 90.9%, Disagree – 3.0%, Abstain – 6.1% (Unanimous Consensus)