Choosing Antimicrobials for Bone Cement: Best Options and Critical Considerations

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INTRODUCTION

Periprosthetic joint infection (PJI) is a rare but serious complication. A fundamental aspect of PJI treatment is the use of bone cement enriched with antibiotics or antifungal agents. For therapeutic use, it is often necessary to manually mix active ingredients with commercially produced bone cements. However, the potential problems arising from this manual mixing have not yet been comprehensively documented. The aim of this study is to investigate the effects of additional homogenization through dry mixing and to provide an overview of the possibilities for mixing in antimicrobial substances, including their optimal dosage.

METHODS

Literature Review: Current evidence on manual antimicrobial admixing into PMMA cement was systematically reviewed, focusing on antimicrobial release, mechanical properties, homogeneity, handling characteristics, and clinical applicability in PJI treatment. Findings from in vitro studies, clinical reports, consensus recommendations, and reference literature were synthesized into practical recommendations for orthopedic use [1].

Experimental Assessment: Four vancomycin-loaded PMMA cement formulations with and without additional dry mixing in a vacuum-mixing cartridge were compared with commercial antibiotic-loaded cements. Mechanical performance, antibiotic elution, and mixing system abrasion were evaluated [1].

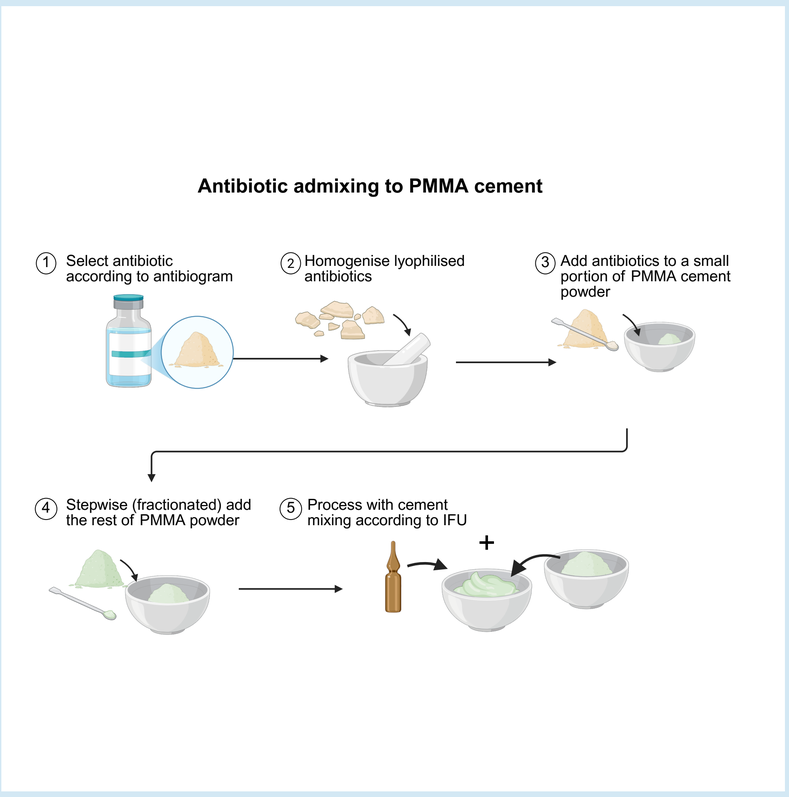
CONCLUSION

Manual antimicrobial admixing should be reserved for specific clinical indications. Additional dry mixing in a cartridge system is not recommended, as it offers no measurable benefit while increasing the risk of cartridge abrasion. Evidence-based antimicrobial selection and standardized mixing procedures are essential to ensure adequate antibiotic elution and mechanical stability of PMMA cements.

- **Never homogenize antibiotic powder dry in a cartridge mixing system** as this could potentially increse the abrasion risk
- **Prepare PMMA cement for spacer without vacuum** as vacuum mixing could reduce antibiotic elution
- **Never add liquid antibiotics to the powder** as this could interfere with the cement matrix and potentially weaken it
- **Pay attention to the quality of the anti-infective substance** as this could come with potential filling substances reducing the total amount of active substance
- **Use sterile antibiotic powder** to reduce the risk for potential contamination

RESULTS

The main outcome of this study is an evidence-based admixing guide for antimicrobial-loaded PMMA cements. Through comprehensive analysis of the available literature, recommendations were compiled for the most relevant clinical scenarios encountered in PJI, including infections caused by resistant Gram-positive bacteria, Gram-negative pathogens, and fungi. The resulting overview integrates information on antimicrobial selection, dosage, commercial availability, handling, mechanical compatibility, and elution performance, providing practical guidance for the safe manual preparation of antimicrobial-loaded bone cement. Particular importance was assigned to achieving a homogeneous distribution of antimicrobial agents through a fractionated admixing approach. This method supports uniform distribution of the active substance. Supporting laboratory investigations showed no benefit of additional dry mixing in a cartridge for cement homogeneity, antibiotic release, or mechanical performance, while demonstrating increased abrasion of the mixing cartridges. These findings reinforce the recommendation to use careful fractionated admixing in an open bowl without an additional dry-mixing in a vacuum cartridge.



Recommendation for manually admixing anti-infective agents to PMMA bone cement following the fractionated admixing protocol.

Clinical situation/ pathogen	Antimicrobials	Commercially available/ manual admixing	Dosage fixation cement	Dosage spacer cement	Admixing procedure	Mechanical properties	Synergistic elution effect	Remarks
Susceptible pathogen unknown	Gentamicin + Clindamycin	COPAL G + C, Refobacin revision	1 g + 1 g	1 g + 1 g				Clindamycin is not available as sterile powder
	Gentamicin + Clindamycin + Vancomycin			1 g + 1 g + 2 g				Source and quality of vancomycin is decisive
Methicillin-resistant: *Staphylococcus epidermidis* (MRSE) *Staphylococcus aureus* (MRSA) Oxacillin-resistant: *Staphylococcus aureus* (ORSA) *Enterococci*	Gentamicin + Vancomyin	COPAL G + V, VancoGenx	0.5 g + 2 g	0.5 g + 2 g				Source and quality of vancomycin is decisive
	Gentamicin + Daptomycin	Admixing	0.5 g + 2 g	0.5 g + 3 g				Easy admixing of daptomycin
Vancomycin-resistant: *Enterococci* (VRE) *Staphylcoccus aureus* (VRSA/VISA)	Gentamicin + Linezolid	Admixing	0.5 g + 1 g	0.5–1 g + 2 g				Easy admixing of linzelolid Linezolid is costly
	Gentamicin + Daptomycin	Admixing	0.5 g + 2 g	0.5–1 g + 3 g				Easy admixing of daptomycin
	Gentamicin + Fosfomycin sodium	Admixing	0.5 g + 2 g	0.5–1 g + 2–4 g				Dosage form important, prefer sodium
	Gentamicin + Tigecycline	Admixing	0.5 g + 0.5 g	0.5–1 g + 1 g				Tigecycline stains PMMA powder orange-brown
Resistant gram-negative bacteria for example: *Escherichia coli* *Klebsiella* *Enterobacter* *Pseudomonas* spp.	Gentamicin + Colistin	Antibiotic simplex E + C	0.5 + 5–10 Mio IU	0.5–1 + 10–20 Mio IU				Antibiotic Simplex E + C no longer available, use colistin-sodium or colistin-sulfate for admixing, small ampoules with powder
	Gentamicin + Fosfomycin sodium	Admixing	0.5 g + 2 g	0.5 g + 2–4 g				Formulation is important; recommendation to prefer fosfomycin sodium
	Gentamicin + Meropenem	Admixing	0.5 g + 2 g	0.5–1 g + 3 g				Easy admixing of meropenem
	Gentamicin + Ciprofloxacin	Admixing	0.5 g + 2 g	0.5–1 g + 3 g				Recommendation to prefer ciprofloxacin salt over pure ciprofloxacin
Fungi for example: *Candida* spp. *Aspergillus* spp.	Gentamicin + Amphotericin B	Admixing	0.5 g + 200 mg	0.5–1 g + 400 mg				PMMA cement is stained orange-brown To achieve a concentration of 200 mg use 4 × 1.3 g of amphotericin B
	Gentamicin + Voriconazole	Admixing	0.5 g + 200 mg	0.5–1 g + 400 mg				To achieve a concentration of 200 mg use 3.5 g of voriconazole

This table offers on overview on the most common germs and corresponding anti-infectives as well as recommendations for admixing. Clinical situation and anti-infective dosages according to PIF Pocket Guide [2]. Green, Easy admixing/good mechanical properties/synergistic elution effect; yellow, Careful admixing/reduced mechanical properties/reduced synergistic elution effect; red, Difficult admixing/limited mechancial properties/ limited synergistic elution effect.

[1] Humez, M., Citak, M., Luck, S., Linke, P., Gehrke, T., Paul, C. and Kühn, K.-D. (2025), Enhancing PMMA Cements With Manually Added Antimicrobial Agents. APMIS, 133: e70029. https://doi.org/10.1111/apm.70029
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