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CORR Insights®: Phosphatidylcholine Coatings Deliver Local Antimicrobials and Reduce Infection in a Murine Model: A Preliminary Study

Arnold J. Suda MD, PhD

Where Are We Now?

Prosthetic joint infection (PJI) therapy remains one of the most challenging and expensive diagnoses to treat in orthopaedic surgery because implant preservation is difficult to achieve, and often is unsuccessful [11]. Resistant biofilm on

an implant's surface makes standard systemic antibiotic treatment ineffective. Because of this, we need more research on approaches to hinder or prevent bacterial biofilm growth. Recently, different approaches regarding biofilm inhibition with a phospholipid and unsaturated fatty acid have shown promising results [6, 7]. In vivo PJI models found that the phospholipid phosphatidylcholine reduced bacterial colony-forming units (CFUs), and the biofilm dispersal agent cis-2-decenoic acid (C2DA) inhibited *Staphylococcus aureus* biofilm in vitro [6, 7]. Pre-established catheter biofilms were eradicated using a combination of C2DA and antibiotics

[12]. These substances may be useful during PJI treatment in combination with antibiotics.

In the current study, Harris and colleagues extended their previous work [4–7] by investigating (1) the in vitro elution profiles of amikacin and C2DA from phosphatidylcholine-coated coupons, (2) the effect of C2DA on the amount of amikacin needed for bacterial inhibition, and (3) the effect of adding amikacin and C2DA regarding CFUs in wires and bone compared with phosphatidylcholine coatings alone in a murine model of PJI. The authors found that all tested eluate samples inhibited *Pseudomonas aeruginosa*. The inhibition of *S aureus* was dependent on the ratio of amikacin combined with C2DA. All groups achieved bacterial clearance on wires, whereas the C2DA-alone and amikacin-alone coatings also cleared all CFUs from the bone. The results of this preliminary study bring us closer to the ultimate goal: The invention of biofilm-resistant implant coatings.

This CORR Insights® is a commentary on the article "Phosphatidylcholine Coatings Deliver Local Antimicrobials and Reduce Infection in a Murine Model: A Preliminary Study" by Harris and colleagues available at: DOI: 10.1007/s11999-016-5211-7.

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This *CORR Insights®* comment refers to the article available at DOI: 10.1007/s11999-016-5211-7.

A. J. Suda MD, PhD (✉)
University Medical Center Mannheim,
Medical Faculty Mannheim of
Heidelberg University, Theodor-Kutzer-
Ufer 1-3, Mannheim 68167, Germany
e-mail: arnoldsuda@yahoo.com

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Where Do We Need To Go?

The use of local biofilm-inhibiting agents seem promising from the safety standpoint; for example, gentamicin-coated nails do not show systemic antibiotic release [1, 3, 9]. However, researchers have not come to a consensus regarding the need for local antibiotics in the treatment of PJI for infected TKAs [10, 13, 14]. In addition, we need to know whether local antibiotics or agents such as phosphatidylcholine or C2DA can withstand the coating process of implants as nails, plates, or artificial joints without losing their antimicrobial effects. And importantly, synergistic effects of antibiotics and C2DA were mentioned in the discussion of this study and could not be completely excluded; this topic needs further exploration.

Research in this field is urgently needed, as avoiding PJI right from the start is the best option both for the patient and the healthcare system. Specifically, to confirm the result of the preliminary studies we now have, we need basic research studies focusing on (1) antimicrobial agents or antibiotic-eluting implant coatings and (2) antiadhesive implant surfaces.

How Do We Get There?

Implant coatings have a limited antibiotic release, which can promote

resistant strains. Using C2DA or phosphatidylcholine for these coatings could be a promising direction for a randomized in vivo study comparing no coating to coating with the antimicrobial peptide OP-145, which was shown to be useful in the prevention of biomaterial-associated infections [2]. Additionally, antibiotic-loaded, polymer-lipid encapsulation matrix coating of orthopaedic implants is a promising approach and should be pursued in blinded in vivo studies [8]. These substances must prove their resistance to temperature of bone cement or mechanical load before we can introduce them into orthopaedic surgery.

References

1. Back DA, Bormann N, Calafi A, Zech J, Garbe LA, Muller M, Willy C, Schmidmaier G, Wildemann B. Testing of antibiotic releasing implant coatings to fight bacteria in combat-associated osteomyelitis - an in-vitro study. *Int Orthop*. 2016;40:1039–1047.
2. de Breij A, Riool M, Kwakman PH, de Boer L, Cordfunke RA, Drijfhout JW, Cohen O, Emanuel N, Zaat SA, Nibbering PH, Moriarty TF. Prevention of *Staphylococcus aureus* biomaterial-associated infections using a polymer-lipid coating containing the antimicrobial peptide OP-145. *J Control Release*. 2016;222:1–8.
3. Diefenbeck M, Muckley T, Hofmann GO. Prophylaxis and treatment of implant-related infections by local application of antibiotics. *Injury*. 2006;37 Suppl 2:S95–104.
4. Jennings JA, Beenken KE, Parker AC, Smith JK, Courtney HS, Smeltzer MS, Haggard WO. Polymicrobial biofilm inhibition effects of acetate-buffered chitosan sponge delivery device. *Macromol Biosci*. 2016;16:591–598.
5. Jennings JA, Beenken KE, Skinner RA, Meeker DG, Smeltzer MS, Haggard WO, Troxel KS. Antibiotic-loaded phosphatidylcholine inhibits staphylococcal bone infection. *World J Orthop*. 2016;7:467–474.
6. Jennings JA, Carpenter DP, Troxel KS, Beenken KE, Smeltzer MS, Courtney HS, Haggard WO. Novel antibiotic-loaded point-of-care implant coating inhibits biofilm. *Clin Orthop Relat Res*. 2015;473:2270–2282.
7. Jennings JA, Courtney HS, Haggard WO. Cis-2-decenoic acid inhibits *S. aureus* growth and biofilm in vitro: a pilot study. *Clin Orthop Relat Res*. 2012;470:2663–2670.
8. Metsemakers WJ, Emanuel N, Cohen O, Reichart M, Potapova I, Schmid T, Segal D, Riool M, Kwakman PH, de Boer L, de Breij A, Nibbering PH, Richards RG, Zaat SA, Moriarty TF. A doxycycline-loaded polymer-lipid encapsulation matrix coating for the prevention of implant-related osteomyelitis due to doxycycline-resistant methicillin-resistant *Staphylococcus aureus*. *J Control Release*. 2015;209:47–56.
9. Moghaddam A, Graeser V, Westhauer F, Dapunt U, Kamradt T, Woerner SM, Schmidmaier G. Patients' safety: is there a systemic release of

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- gentamicin by gentamicin-coated tibia nails in clinical use? *Ther Clin Risk Manag.* 2016;12:1387–1393.
10. Parvizi J, Gehrke T. International consensus on periprosthetic joint infection: let cumulative wisdom be a guide. *J Bone Joint Surg Am.* 2014;96:441.
 11. Parvizi J, Haddad FS. Periprosthetic joint infection: The last frontier. *Bone Joint J.* 2015;97-B:1157–1158.
 12. Rahmani-Badi A, Sepehr S, Mohammadi P, Soudi MR, Babaie-Naiej H, Fallahi H. A combination of cis-2-decenoic acid and antibiotics eradicates pre-established catheter-associated biofilms. *J Med Microbiol.* 2014;63:1509–1516.
 13. Whiteside LA, Nayfeh TA, LaZear R, Roy ME. Reinfected revised TKA resolves with an aggressive protocol and antibiotic infusion. *Clin Orthop Relat Res.* 2012;470:236–243.
 14. Whiteside LA, Peppers M, Nayfeh TA, Roy ME. Methicillin-resistant *Staphylococcus aureus* in TKA treated with revision and direct intra-articular antibiotic infusion. *Clin Orthop Relat Res.* 2011;469:26–33.