Alberta Health Services Pharmacy Services

Issue 23 – November 2022

Antimicrobial Stewardship Backgrounder

Bacitracin and Risks Associated with Use in Surgery

BOTTOM LINE:

- **Bacitracin for injection is NOT indicated in surgical irrigation solutions**
- **Bacitracin for injection is NOT indicated for pre-soaking of medical devices or implants prior to surgery.**
- **Bacitracin, when used in irrigation solutions, has been associated with sudden, severe, potentially life-threatening anaphylactic reactions and nephrotoxicity.**

Background:

- The intention of intraoperative surgical site irrigation is to reduce the risk of surgical site infections (SSIs) by diluting or physically removing cellular debris, necrotic tissue, and surface bacteria.[8-10]
- Off-label use of bacitracin for intraoperative irrigation, device, and implant pre-soaking is variable but widespread, including in AHS facilities.[3,9]
- In January of 2020, the US Food and Drug Administration (FDA) requested all manufacturers of bacitracin for injection voluntarily withdraw their product from the market.[4] After completing a safety review, Health Canada decided to keep bacitracin on the market but released a statement which concluded there may be a link between bacitracin for injection and the risk of anaphylaxis and nephrotoxicity.[1]

Efficacy:

- Antimicrobial activity requires sufficient contact time to allow the antibiotic agent used for irrigation to bind to its target site within the cell membrane.[19] One in vitro study demonstrated that most antibiotic irrigation solutions required 30 minutes of exposure for a reliable antibiotic effect.[20] Antimicrobial activity also depends on persistent drug concentrations that exceed the minimum inhibitory concentration (MIC) 90.[19] Neither of these are achieved with surgical site antibiotic irrigation where the solution is quickly flushed away.
- There remains a significant amount of variation in the irrigation solution used, additives, volume, and delivery method between surgery practices.[8]
- In general, high quality evidence to support the use of ANY intraoperative antimicrobial irrigations to prevent SSIs is lacking.[3,8,10-15] Randomized controlled trials and systematic reviews are often underpowered and contain a high risk of bias and heterogeneity.[10-15] For bacitracin irrigation specifically, published evidence consists of older, retrospective, observational studies comparing bacitracin use to saline or soap irrigation.[9]
- Published clinical practice guidelines do not recommend the use of antibiotic irrigations due to insufficient and low quality evidence.[3,9]

Guideline	Recommendation
AHS Surgical Prophylaxis Recommendations[5]	AHS Surgical Prophylaxis recommendations do not support surgical irrigation with antibiotic solutions
ASHP/IDSA/SIS/SHEA 2013[6]	Routine use of antibacterial irrigation solutions cannot be recommended due to insufficient evidence
WHO 2016[16]	Antibiotic incisional wound irrigation should not be done for the purpose of preventing SSIs.
NICE 2019 (updated 2020)[17]	Advised not to use wound irrigation or intra-cavity lavage to reduce the risk of surgical site infection
CDC 2017[18]	No recommendation made; unresolved issue

Abbreviations: AHS: Alberta Health Services; ASHP: American Society of Health-System Pharmacists; IDSA: Infectious Diseases Society of America; SIS: Surgical Infection Society; SHEA: Society for Healthcare Epidemiology of America; WHO: World Health Organization; NICE: National Institute for Health and Care Excellence; CDC: Centers for Disease Control;

Safety:

- Several case reports have documented anaphylactic reactions from use as bacitracin surgical irrigation.[1,4,7,21,22] These reactions typically occur a few minutes following bacitracin irrigation and most commonly involve a hypotensive response with or without cutaneous or pulmonary signs of anaphylaxis.

Prepared by: Sara Kluthe, 4th year Pharmacy Student; Sara.Kluthe@albertahealthservices.ca
Reviewed by: Dr. Tara Klassen, PhD Research Scientist Surgery SCN, and Lynora M Saxinger, MD, FRCPC, CTropMed, Co-chair Antimicrobial Stewardship Committee, AHS

There have been cases where the reaction has progressed to cardiac arrest, even in the absence of skin redness or a rash.[7,21] The reactions tend to occur with minimal bacitracin exposure which indicates that prior exposure may result in bacitracin sensitivity and anaphylactic reactions upon re-exposure.[21,22]

- Health Canada additionally warns that **bacitracin is contraindicated in patients with impaired renal function, including those taking nephrotoxic drugs**.[1]
- Other concerns identified include inadvertent Intravenous administration of irrigation solutions, calculation or dilution errors resulting in incorrect dose, contamination of the solutions mixed in the operating room and emergence of antibiotic resistance with the use of intraoperative antibiotic irrigations.[3-4,9]

Sustainability:

- Annual expenditure of bacitracin 50,000 unit injection in AHS is $117,150 (DOSE data 2022 fiscal). If bacitracin is removed from the AHS Provincial Drug Formulary there is potential for significant savings to AHS drug budget.
- For alternatives to bacitracin irrigation, emerging evidence supports evaluation of a number of alternative antiseptic solutions if irrigation is performed.[10,16] Refer to the AHS Surgical Prophylaxis Guidelines for preoperative antibiotic prophylaxis.[5]

References:

1. Health Canada. Summary Safety Review - Bacitracin for injection products - Health Canada. Internet Document: Dec 21, 2020. Available from https://hpr-rps.hres.ca/reg-content/summary-safety-review-detail.php?lang=en&linkID=SSR00250
2. Prescribing Information. BaciJect. SteriMax Inc. Product Monograph. Date of revision: June 5, 2020. PRESCRIBING INFORMATION (sterimaxinc.com)
3. Meng L, Deresinski S, Holubar M. Intraoperative bacitracin irrigations for the prevention of surgical site infections-Consider the alternatives. Infect Control Hosp Epidemiol. 2020 Jul;41(7):831-832. doi: 10.1017/ice.2020.67. Epub 2020 May 5. PMID: 32366347
4. Food and Drugs Administration. FDA requests withdrawal of bacitracin for injection from market. Internet document: Jan. 31, 2020. Available from: https://www.fda.gov/drugs/drug-safety-and-availability/fda-requests-withdrawal-bacitracin-injection-market
5. AHS Recommended Drug Regimens for Surgical Prophylaxis December 2018. https://www.bugsanddrugs.org/AE6C8898-C0FA-4FDE-82EA-B7BC0556A30F
6. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, Fish DN, Napolitano LM, Sawyer RG, Slain D, Steinberg JP, Weinstein RA; American Society of Health-System Pharmacists (ASHP); Infectious Diseases Society of America (IDSA); Surgical Infection Society (SIS); Society for Healthcare Epidemiology of America (SHEA). Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt). 2013 Feb;14(1):73-156. doi: 10.1089/sur.2013.9999. Epub 2013 Mar 5. PMID: 23461695.
7. Greenberg SB, Deshur M, Khavkin Y, Karaikovic E, Vender J. Successful Resuscitation of a Patient Who Developed Cardiac Arrest from Pulsed Saline Bacitracin Lavage during Thoracic Laminectomy and Fusion. Journal of Clinical Anesthesia 20, no. 4 (2008): 294–96.
8. Barnes S, Spencer M, Graham D, Johnson HB. Surgical wound irrigation: a call for evidence-based standardization of practice. Am J Infect Control. 2014 May;42(5):525-9. doi: 10.1016/j.ajic.2014.01.012. PMID: 24773788.
9. Edmiston CE Jr, Leaper D, Spencer M, Truitt K, Litz Fauerbach L, Graham D, Johnson HB. Considering a new domain for antimicrobial stewardship: Topical antibiotics in the open surgical wound. Am J Infect Control. 2017 Nov 1;45(11):1259-1266. doi: 10.1016/j.ajic.2017.04.012. Epub 2017 Jun 5. PMID: 28596018
10. Abboud K, Blee J, Shah P. Antibiotic irrigation solutions for prevention of surgical site infections: A call to action. AM J Health-System Pharmacists. 2020. Doi: 10.1093/ajhp/zxaa316. PMID: 33079184
11. Norman G, Atkinson RA, Smith TA, Rowlands C, Rithalia AD, Crosbie EJ, Dumville JC. Intracavity lavage and wound irrigation for prevention of surgical site infection. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD012234. DOI: 10.1002/14651858.CD012234.pub2
12. Mueller TC, Loos M, Haller B, et al. Intra-operative wound irrigation to reduce surgical site infections after abdominal surgery: A systematic review and meta-analysis. Langenbecks Arch Surg 2015; 400:167–181.
13. Wood T, Ekhtiari S, Mundi R, et al. (April 24, 2020) The Effect of Irrigation Fluid on Periprosthetic Joint Infection in Total Hip and Knee Arthroplasty: A Systematic Review and Meta-Analysis. Cureus 12(4): e7813. DOI 10.7759/cureus.7813
14. de Jonge SW, Boldingh QJJ, Solomkin JS, Allegranzi B, Egger M, Dellinger EP, Boermeester MA. Systematic Review and Meta-Analysis of Randomized Controlled Trials Evaluating Prophylactic Intra-Operative Wound Irrigation for the Prevention of Surgical Site Infections. Surg Infect (Larchmt). 2017 May/Jun;18(4):508-519. doi: 10.1089/sur.2016.272. Epub 2017 Apr 27. PMID: 28448203
15. Thom H, Norman G, Welton NJ, Crosbie EJ, Blazeby J, Dumville JC. Intra-Cavity Lavage and Wound Irrigation for Prevention of Surgical Site Infection: Systematic Review and Network Meta-Analysis. Surg Infect (Larchmt). 2021 Mar;22(2):144-167. doi: 10.1089/sur.2019.318. Epub 2020 Apr 29. PMID: 32352895.
16. Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F, Gomes SM, Gans S, Wallert ED, Wu X, Abbas M, Boermeester MA, Dellinger EP, Egger M, Gastmeier P, Guirao X, Ren J, Pittet D, Solomkin JS; WHO Guidelines Development Group. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis. 2016 Dec;16(12): e288-e303. doi: 10.1016/S1473-3099(16)30402-9. Epub 2016 Nov 2. PMID: 27816414
17. Surgical site infections: prevention and treatment. London: National Institute for Health and Care Excellence (UK); 2020 Aug 19. (NICE Guideline, No. 125.) Available from: https://www.ncbi.nlm.nih.gov/books/NBK542473/
18. Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, Reinke CE, Morgan S, Solomkin JS, Mazuski JE, Dellinger EP, Itani KMF, Berbari EF, Segreti J, Parvizi J, Blanchard J, Allen G, Kluytmans JAJW, Donlan R, Schecter WP; Healthcare Infection Control Practices Advisory Committee. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. JAMA Surg. 2017 Aug 1;152(8):784-791. doi: 10.1001/jamasurg.2017.0904. Erratum in: JAMA Surg. 2017 Aug 1;152(8):803. PMID: 28467526
19. Edmiston CE Jr, Spencer M, Leaper D. Antiseptic Irrigation as an Effective Interventional Strategy for Reducing the Risk of Surgical Site Infections. Surg Infect (Larchmt). 2018 Nov/Dec;19(8):774-780. doi: 10.1089/sur.2018.156. Epub 2018 Oct 9. PMID: 30300563.
20. Zhadan O, Becker H. Surgical Site Irrigation in Plastic Surgery. Aesthet Surg J. 2018 Feb 15;38(3):265-273. doi: 10.1093/asj/sjx171. PMID: 29087441
21. Damm S. Intraoperative anaphylaxis associated with bacitracin irrigation. Am J Health Syst Pharm. 2011 Feb 15;68(4):323-7. doi: 10.2146/ajhp090238. PMID: 21289327.
22. Blas M, Briesacher KS, Lobato EB. Bacitracin Irrigation: A Cause of Anaphylaxis in the Operating Room. Anesth Analg. 2000 May 30; 91:1027-8. doi: 10.1097/539 PMID: 11004070

Prepared by: Sara Kluthe, 4th year Pharmacy Student; Sara.Kluthe@albertahealthservices.ca
Reviewed by: Dr. Tara Klassen, PhD Research Scientist Surgery SCN, and Lynora M Saxinger, MD, FRCPC, CTropMed, Co-chair Antimicrobial Stewardship Committee, AHS