higher risk of developing PJI in a subsequent THA or TKA (10 of 90, versus 0 of 90 in the control group; risk rato: 21.00; 95% confidence interval (CI), 1.25-353.08; p = 0.04). The authors found that a second PJI occurred more frequently in those whose initial infection was by a staphylococcal species (odds ratio (OR), 4.26 p = 0.04). The infecting organisms were the same species in the first and second PJI in 40% of cases, and all four of these were caused by Staphylococci.

Based on the available data, it appears that patients with a prior PJI who are undergoing elective arthroplasty are at higher risk of subsequent infection. The infecting organism for the second joint is most of the time same as the first infecting organism. Taken together, we feel that antibiotic prophylaxis for patients with a prior PJI who are undergoing an elective primary or revision arthroplasty needs to be altered. These patients may require administration of an alternative or additional antibiotic(s). For example, patients with a prior PJI by a gram-negative organism should receive prophylactic antibiotics against gram-negative bacteria. The same applies to patients with a prior MRSA infection and so on.

REFERENCES

[1] Murray RP, Bourne MH, Fitzgerald RH. Metachronous infections in patients who have had more than one total joint arthroplasty. J Bone Joint Surg Am. 1991;73:1469–1474.
[2] Parvizi J, Azzam K, Ghanem E, et al. Periprosthetic infection due to resistant staphylococci: serious problems on the horizon. Clin Orthop Relat Res. 2009;467:1732–1739.
[3] Leung F, Richards CJ, Garbuz Ds, et al. Two-stage total hip arthroplasty: how often does it control methicillin-resistant infection? Clin Orthop Relat Res. 2011;469:1009–1015.
[4] Luessenhop CP, Higgins LD, Brause BD, Ranawat CS. Multiple prosthetic infecions after total joint arthroplasty. Risk factor analysis. J Arthroplasty. 1996;11:862-868.
[5] Jafari SM, Casper DS, Restrepo C, Zmistowski B, Parvizi J, Sharkey PF. Periprosthetic joint infection: are patients with multiple prosthetic joints at risk? J Arthroplasty. 2012; 27:877–880.
[6] Zmistowski B, Tetreault MW, Alijanipour P, Chen AF, Della Valle CJ, Parvizi J. Recurrent periprosthetic joint infection: persistent or new infection? J Arthroplasty. 2013;28:1486–1489.
[7] Bedair H, Goyal N, Dietz MJ, Urish K, Hansen V, Manrique J, et al. A History of treated periprosthetic joint infection increases the risk of subsequent different site infection. Clin Orthop. 2015;473:2300–2304.

Authors: Jan Erik Berdal, Ibrahim Tuncay

QUESTION 7: Should prophylactic antibiotic therapy be administered for an extended duration in patients admitted to the Intensive Care Unit (ICU)?

RECOMMENDATION: Surgical prophylactic antibiotic therapy should not be administered for an extended duration in patients admitted to the ICU.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 82%, Disagree: 13%, Abstain: 5% (Super Majority, Strong Consensus)

RATIONALE

The literature on surgical site infections (SSIs) classifies SSI risk factors into intrinsic (patient) related (e.g., age and underlying morbidity) and extrinsic (procedure) related (procedure, facility, pre-and intraoperative factors), both being either modifiable or not [1]. Admittance to the ICU is not treated as an independent risk factor, although risk factors for SSIs and risk factors for ICU admittance are correlated (age, co-morbidity, complexity of procedure). Using the published search algorithm from the World Health Organization (WHO) guideline's literature review and narrowing it with the term "ICU" and expanding it with the term "observational study," 180 articles were retrieved from October 1, 2015 until present (PubMed 39, Embase 84, Central 57). All abstracts were screened, but none found relevant for the question of extending antibiotic duration in patients admitted to the ICU. Using the unaltered WHO search algorithm (without narrowing with "ICU" and expanding with "observational study"), another 23 PubMed articles not covered within the first search were identified, but none of the screened abstracts were relevant. An unsystematic search in the PubMed Clinical Queries search was then performed with the terms "(Therapy/Broad [filter]) AND (antibiotic prophylaxis extended)" returning 245 articles. All titles were screened and abstracts of putative relevance reviewed and none were found to be relevant. The 34 articles retrieved with a modified search term (Therapy/Broad [filter]) AND (antibiotic prophylaxis prolonged ICU) were not found to be relevant either. Thus, no studies were found examining extended antibiotic prophylaxis in ICU patients when these patients are considered as a separate patient category and there are no data to support or refute an extended duration for preventing SSIs solely based on the admittance to the ICU.

However, ICU patients are included in the core randomized controlled trials (RCTs) showing no benefit of extending antibiotic prophylaxis past wound closure [2,3] albeit not specifically for arthroplasty patients. Since the publication of the Proceedings of the International Consensus Meeting on Periprosthetic Joint Infections in 2013, three major literature reviews and guidelines on prevention of SSI have been published from WHO [2], Centers for Disease Control and Preventiopn (CDC) [3], and the American College of Surgeons and Surgical Infection Society (ACS/SIS) [1], respectively. The CDC and WHO guidelines agree on not extending prophylaxis past wound closure based on a comprehensive systematic literature review, but the strength of the data supporting the recommendation for arthroplasty have been questioned [4–11]. The ACS/SIS makes an exception for prophylactic antibiotics past wound closure for joint arthroplasty, on the grounds that optimal antibiotic therapy for these patients remains unknown, but refers to the American Society of Health-System Pharmacists (ASHP); Infectious Diseases Society of America (IDSA); Surgical Infection Society (SIS); and the Society for Healthcare Epidemiology of America (SHEA) guidelines for a total antibiotic prophylaxis duration ≤ 24 hours [12]. A recently published meta-analysis and review on postoperative antibiotic prophylaxis in knee and hip arthroplasty did not find evidence to show efficacy of extended antibiotic prophylaxis for the prevention of SSI in patients undergoing total hip or knee arthro-

plasty. It did however question the quality of the existing evidence and call for new and sufficiently powered RCTs to settle the issue [12]. None of the guidelines or the extensive literature reviews underpinning them thus makes a distinction or specific recommendation for patients admitted to the ICU in general or for use of extended antibiotic prophylaxis for ICU patients in particular. However, ICU patients are included in the core RCTs forming the basis for the strong recommendations of not extending antibiotic prophylaxis after completion of the operation.

ICUs are heterogeneous and ICU capacity varies greatly across hospitals and countries. Consequently, both patient morbidity and hospital policies for ICU admittance will vary, making studies examining extended antibiotic prophylaxis based on ICU admittance unlikely. Should they be undertaken, their external validity would for the above-mentioned reasons be questionable.

The purpose of prophylactic antibiotic therapy in orthopaedic surgery is to prevent SSIs, for which a narrow-acting antibiotic with gram-positive coverage is a proven and sufficient option [13]. Prevention of remote infections in patients admitted to the ICU would have required a different prophylactic approach, including administration of broad-spectrum antibiotics and selective digestive decontamination (SDD), as opposed to the narrow spectrum antibiotics for SSI prevention. Although there are some data to support such a strategy, mainly from ICUs with low levels of antibiotic resistance [14], it remains highly controversial due to concerns of long- term resistance promotion and disturbance to the gut microbiome [15]. There is currently insufficient evidence to recommend its use in settings with high levels of antibiotic resistance [16]. Though an in-depth discussion of the issue is beyond the scope of the assigned question, the increased sense of urgency regarding resistance prevention following the 2014 WHO report on global resistance [17] speaks strongly against adoption of this strategy.

In addition to high awareness, prompt diagnostic workup and early initiations of broad empiric antibiotic therapy are the core interventions for reducing infection related complications in the ICU [18]. The continuation of a narrow-acting antibiotic therapy from the operating theater into the ICU may give a false sense of security and both obscure and delay these interventions, or even harm patients by promoting antimicrobial-resistant bacteria [19,20].

Arguably, the immunosuppressed state following surgery and trauma could be enhanced in patients ill enough to require treatment in the ICU, thus justifying implementation of antibiotic prophylaxis recommendation for immunosuppressed patients. However, despite not identifying studies addressing extended surgical antimicrobial prophylaxis (SAP) in arthroplasty for immunocompromised patients, the CDC guidelines give a strong recommendation (category 1a) against extended SAP in the immunocompromised patients based on their inclusion in the core RCTs with high quality evidence for SAP ≤ 24 hours postoperatively [21].

In an editorial commenting on a survey of 67 ICUs finding 50% of antibiotic prescriptions being continued beyond 72 hours despite absence of a definitive infectious source [22], the editor states that "there is a pervasive belief that an error of commission" (continuation of empiric antibiotics in the absence of evidence of infection) "is somehow better or safer than an error of omission" (ceasing antibiotic therapy when there is some chance–however slim–that the patient will benefit) [23]. This statement also applies fittingly to the question of extended prophylaxis in patients admitted to ICU; with a real threat of running out of effective antibiotics due to indiscriminate use, extending prophylaxis on the sole ground of ICU admittance should be avoided as there is neither theoretical rationale nor clinical evidence to support the practice.

REFERENCES

[1] Ban KA, Minei JP, Laronga C, Harbrecht BG, Jensen EH, Fry DE, et al. American College of Surgeons and Surgical Infection Society: surgical site infection guidelines: 2016 Update. J Am Coll Surg. 2017;224:59–74. doi:10.1016/j.jamcollsurg.2016.10.029.

[2] World Health Organization. Global guidelines for the prevention of surgical site infection. 2016. http://apps.who.int/iris/bitstream/handle/10665/250680/9789241549882-eng.pdf;jsessionid=1E47C47E25A5C6CBFB6F792009A84054?sequence=1.

[3] Leaper DJ, Edmiston CE. World Health Organization: global guidelines for the prevention of surgical site infection. J Hosp Infect. 2017;95:135–136. doi:10.1016/j.jhin.2016.12.016.

[4] Ali M, Raza A. Role of single dose antibiotic prophylaxis in clean orthopedic surgery. J Coll Physicians Surg Pak. 2006;16:45–48. doi:1.2006/JCPSP.4548.

[5] Buckley R, Hughes GN, Snodgrass T, Huchcroft SA. Perioperative cefazolin prophylaxis in hip fracture surgery. Can J Surg. 1990;33:122–127.

[6] Garotta F, Pamparana F. Antimicrobial prophylaxis with ceftizoxime versus cefuroxime in orthopedic surgery. Ceftizoxime Orthopedic Surgery Italian Study Group. J Chemother. 1991;3:34–35.

[7] Gatell JM, Garcia S, Lozano L, Soriano E, Ramon R, SanMiguel JG. Perioperative cefamandole prophylaxis against infections. J Bone Joint Surg Am. 1987;69:1189–1193.

[8] Ritter MA, Campbell E, Keating EM, Faris PM. Comparison of intraoperative versus 24 hour antibiotic prophylaxis in total joint replacement. A controlled prospective study. Orthop Rev. 1989;18:694–696.

[9] Wymenga AB, Hekster YA, Theeuwes A, Muytjens HL, van Horn JR, Slooff TJ. Antibiotic use after cefuroxime prophylaxis in hip and knee joint replacement. Clin Pharmacol Ther. 1991;50:215–220.

[10] Hellbusch LC, Helzer-Julin M, Doran SE, Leibrock LG, Long DJ, Puccioni MJ, et al. Single-dose vs. multiple-dose antibiotic prophylaxis in instrumented lumbar fusion–a prospective study. Surg Neurol. 2008;70:622–627; discussion 627. doi:10.1016/j.surneu.2007.08.017.

[11] Takemoto RC, Lonner B, Andres T, Park J, Ricart-Hoffiz P, Bendo J, et al. Appropriateness of twenty-four-hour antibiotic prophylaxis after spinal surgery in which a drain is utilized: a prospective randomized study. J Bone Joint Surg Am. 2015;97:979–986. doi:10.2106/JBJS.L.00782.

[12] Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;70:195–283. doi:10.2146/ajhp120568.

[13] Thornley P, Evaniew N, Riediger M, Winemaker M, Bhandari M, Ghert M. Postoperative antibiotic prophylaxis in total hip and knee arthroplasty: a systematic review and meta-analysis of randomized controlled trials. CMAJ Open. 2015;3:E338-E343. doi:10.9778/cmajo.20150012.

[14] de Smet AMGA, Kluytmans J a. JW, Cooper BS, Mascini EM, Benus RFJ, van der Werf TS, et al. Decontamination of the digestive tract and oropharynx in ICU patients. N Engl J Med. 2009;360:20–31. doi:10.1056/NEJMoa0800394.

[15] Kollef MH, Micek ST. Rational use of antibiotics in the ICU: balancing stewardship and clinical outcomes. JAMA. 2014;312:1403–1404. doi:10.1001/jama.2014.8427.

[16] Plantinga NL, Bonten MJM. Selective decontamination and antibiotic resistance in ICUs. Crit Care. 2015;19:259. doi:10.1186/s13054-015-0967-9.

[17] World Health Organization. Antimicrobial resistance: global report on surveillance. 2014. http://apps.who.int/iris/bitstream/handle/10665/112642/9789241564748_eng.pdf?sequence=1.

[18] Kollef MH, Sherman G, Ward S, Fraser VJ. Inadequate antimicrobial treatment of infections: a risk factor for hospital mortality among critically ill patients. Chest. 1999;115:462–474.

[19] Terpstra S, Noordhoek GT, Voesten HG, Hendriks B, Degener JE. Rapid emergence of resistant coagulase-negative staphylococci on the skin after antibiotic prophylaxis. J Hosp Infect. 1999;43:195–202. doi:10.1053/jhin.1999.0636.

[20] Hoth JJ, Franklin GA, Stassen NA, Girard SM, Rodriguez RJ, Rodriguez JL. Prophylactic antibiotics adversely affect nosocomial pneumonia in trauma patients. J Trauma. 2003;55:249–54. doi:10.1097/01.TA.0000083334.93868.65.

[21] Berrios-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for Disease Control and Prevention guideline for the prevention of surgical site infection, 2017. JAMA Surg. 2017;152:784–791. doi:10.1001/jamasurg.2017.0904.

[22] Thomas Z, Bandali F, Sankaranarayanan J, Reardon T, Olsen KM, Critical Care Pharmacotherapy Trials Network. A multicenter evaluation of prolonged empiric antibiotic therapy in adult ICUs in the United States. Crit Care Med. 2015;43:2527–2534. doi:10.1097/CCM.0000000000001294.

[23] Rimawi RH. Just say "stop": avoiding prolonged empiric antibiotics. Crit Care Med. 2015;43:2675–2676. doi:10.1097/CCM.0000000000001417.