Disclosures. All authors: No reported disclosures.

287. The Attributable Mortality of Prosthetic Joint Infection After Primary Hip and Knee Arthroplasty Among Medicare Beneficiaries, 2005–2012

Kara Jacobs Silka, MD, MPH1,2; Sarah H. Yi, PhD3; Sujan C. Reddy, MD1,3; James Baggs, PhD3 and John A. Jernigan, MD, MS1,4; Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia. 2Division of Infectious Diseases, Emory University, Atlanta, Georgia. 3Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia. 4Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Session: 54. Bone and Joint Infections
Thursday, October 4, 2018: 12:30 PM

Background. Total hip (THA) and total knee (TKA) arthroplasty are the most common elective surgical procedures performed in the USA. Most are performed in older adults and lead to improved quality of life; however, complications such as prosthetic joint infection (PJI) can occur. Little is known regarding the mortality attributable to PJI after THA or TKA.

Methods. Claims data from the 2004 to 2012 Medicare 5% sample Standard Analytic Files were used to find eligible beneficiaries, with ICD-9-CM procedure codes identifying primary THA (81.51) or primary TKA (81.54), and diagnosis code 996.66 indicating PJI during the year following the procedure. Inclusion criteria included traditional Medicare coverage during the year prior and two years following the procedure and original reason for entitlement due to age. Exclusion criteria included missing surgery date, additional primary procedures within one year, and PJI diagnosis prior or during index stay. The attributable mortality of PJI during the 2 years following primary hip and knee arthroplasty among Medicare beneficiaries was calculated by fitting Kaplan-Meier survival curves and performing a time-dependent analysis based on PJI timing using an Extended Cox Proportional Hazard model.

Results. A total of 248,340 hip and knee arthroplasties were performed on 54.5% Medicare sample beneficiaries between 2005 and 2012. The final cohort included 117,515 arthroplasties (52%); 37,098 (32%) hip, and 80,429 (68%) knee, of which 80,377 (68%) were performed in women and 61,807 (53%) in patients greater than 75 years of age. PJI was diagnosed in one percent of hip (n = 338) and knee (n = 726) arthroplasties, of which 112 (11%) died. The crude mortality rate was 3.2 (95% CI: 2.3, 4.2) and 3.7 (95% CI: 2.9, 4.8) times greater in patients with PJI than without PJI following THA and TKA, respectively. Controlling for comorbid conditions and the time-dependent nature of PJI, the risk of death with PJI was 2.5 (95% CI: 1.9, 3.3) times higher following THA and 2.6 (95% CI: 2.0, 4.3) times higher following TKA than for non-PJI.

Conclusion. Medicare beneficiaries who develop PJI after THA or TKA have an increased risk of death during the first 2 years following the procedure, supporting the importance of better understanding risk factors and preventing PJI following these elective procedures.

Disclosures. All authors: No reported disclosures.
291. Effect of Previous Antibiotic Exposure on the Yield of Bone Biopsy Culture in Patients With Osteomyelitis

Andrew Simms, BSc1; Paul D. Fy, PhD2; Elizabeth Lyden, MS3; Angela Howlett, MSc2; Mark E. Rupp, MD, PhD1; 1University of Nebraska Medical Center, Omaha, Nebraska, 2Pathology and Microbiology, University of Nebraska Medical Center, Omaha, Nebraska, 3Epidemiology, University of Nebraska Medical Center, Omaha, Nebraska, 4Division of Infectious Diseases, University of Nebraska Medical Center, Omaha, Nebraska, 5Infectious Diseases, University of Nebraska Medical Center, Omaha, Nebraska
Session: 54. Bone and Joint Infections
Thursday, October 4, 2018: 12:30 PM

Background. Bone biopsy culture and core needle biopsy are gold standards for the diagnosis of osteomyelitis and are key factors in defining the etiology and treatment of osteomyelitis. There is concern that recent antibiotic exposure will decrease the sensitivity of microbiologic cultures.

Methods. A retrospective analysis was performed of patients who underwent bone biopsy for evaluation of osteomyelitis at the University of Nebraska Medical Center from 2014 to 2017. Microbiological culture data were compared with the number of days of antibiotic treatment the patient received prior to biopsy. Days of antibiotic therapy were divided into quadrants: 0–3 days, 4–7 days, 8–14 days, and >14 days. A perioperative antibiotic regimen was used to determine independent predictors of culture positivity.

Results. A total of 211 patients were studied. Descriptive statistics: 63% male, 85% Caucasian, median age: 55 years, duration of osteomyelitis prior to biopsy: median 39 days (mean 139 days). Location of osteomyelitis: lower extremity 48%, sacral/pelvic 19%, skull/facial 12%, spine 11%, upper extremity/chest 9%. Within 2 weeks prior to biopsy, the median value of the maximum WBC count, ESR, and CRP was 10.5, 66, and 5.7, respectively. A significant negative linear trend between culture positivity and days of antibiotic exposure (P < 0.0001) was observed (Figure 1). The rate of culture positivity was 85.07% for patients diagnosed with osteomyelitis who did not receive antibiotic exposure, 54.69% for patients who received ≤3 days, 16.67% for patients who received 4–7 days, and 7.14% for patients who received >8 days of antibiotics. A peripherally inserted central catheter was a significant positive predictor of culture positivity (P < 0.0017) and clinical diagnosis of osteomyelitis (P = 0.0017) and clinical diagnosis of osteomyelitis (P = 0.0017).

Conclusion. The frequency of TEAEs was high, though not unexpected in this population with many chronic diseases. FA was well-tolerated with few patients experiencing treatment-related AEs leading to study drug discontinuation. FA administered chronically as monotherapy may lead to decreasing susceptibility and treatment failure in some patients; thus, combination therapy is warranted for this indication.

Disclosures. A. Sheets, Melinta Therapeutics: Employee, Salary; D. Graham, Cempra: Grant Investigator, Research grant; R. Darouiche, Cempra: Grant Investigator, Grant recipient; A. Strayer, Melinta Therapeutics, Inc.: Employee and Shareholder, Salary.

250. Safety and Effectiveness of Oral Sodium Fusicidate (Fusicidic Acid) as Chronic Antibiotic Suppressive Therapy in Patients With Staphylococcal Bone or Joint Infections

Amanda Sheets, PhD1; Donald Graham, MD2; Rabih Darouiche, MD3 and Andrew Strayer, PharmD4; 1Clinical Development, Melinta Therapeutics, Inc., Chapel Hill, North Carolina, 2Department of Pathology and Microbiology, University of Nebraska Medical Center, Omaha, Nebraska, 3Clinical, Development, Melinta Therapeutics, Inc., Chapel Hill, North Carolina, 4Clinical Development, Melinta Therapeutics, Inc., Chapel Hill, North Carolina
Session: 54. Bone and Joint Infections
Thursday, October 4, 2018: 12:30 PM

Background. Fusicidic acid (FA) is an anti-staphylococcal agent used to treat chronic bone and joint infections (B&J) due to the availability of an oral formulation and its MRSA activity. Though used widely throughout the world for decades, FA is not approved in the USA.

Methods. To evaluate the safety and effectiveness of FA as chronic suppressive therapy in patients with staphylococcal B&J, we enrolled 30 patients in a prospective, single-arm, multi-center study in the USA. Eligible patients had refractory infections that could not be managed surgically or had not responded to previous antibiotic treatment. In Part A of the study, all patients received 6 months of oral FA treatment. In the first 1–2 weeks, patients could receive a companion antibiotic. Clinical success was based on lack of need for surgery or additional antibiotics. After all patients completed Part A of the study, an interim analysis was performed. In Part B of the study (ongoing), patients who completed Part A and required continued suppressive therapy may continue to receive FA for a total of 24 months.

Results. Most patients (83%) had orthopedic hardware infections. Therapy was considered successful at the 6-month visit in 18 patients (60%). Microbiological persistence was observed in eight patients, with three cases of decreasing FA susceptibility (including one case of resistance). Among 29 patients who experienced a treatment-emergent adverse event (TEAE), the most frequently reported events were: urinary tract infection (n = 9), peripheral edema/swelling (n = 8), nausea/dyspepsia (n = 7). Seven patients experienced TEAEs related to study drug; mild gastrointestinal disorders were most common. Two treatment-related events (unrelated to therapeutic failure) led to discontinuation of study drug.

Conclusion. Patients with refractory B&J have few treatment options. In our study, 60% of infections were effectively suppressed for 6 months with FA treatment. The frequency of TEAEs was high, though not unexpected in this population with many chronic diseases. FA was well-tolerated with few patients experiencing treatment-related AEs leading to study drug discontinuation. FA administered chronically as monotherapy may lead to decreasing susceptibility and treatment failure in some patients; thus, combination therapy is warranted for this indication.

Disclosures. A. Sheets, Melinta Therapeutics: Employee, Salary; D. Graham, Cempra: Grant Investigator, Research grant; R. Darouiche, Cempra: Grant Investigator, Grant recipient; A. Strayer, Melinta Therapeutics, Inc.: Employee and Shareholder, Salary.