

Title: Oral Cephalosporins versus Fluoroquinolones or Sulfamethoxazole-Trimethoprim for Secondary Prophylaxis of Spontaneous Bacterial Peritonitis: A Nationwide Cohort Study

Authors and Institutions: Patty Callahan, PharmD¹, Ashleigh Wallace-Lacey, PharmD¹, Colleen Lewellyan, PharmD¹, Elizabeth Redd, PharmD, BCIDP¹, Jamie Guyer, PharmD, BCDIP¹, Prashant Pandya, DO^{1,2}. 1. Kansas City VA Medical Center; 2. The University of Kansas Health System

Introduction: Secondary prophylaxis of spontaneous bacterial peritonitis (SBP) with either a fluoroquinolone or trimethoprim/sulfamethoxazole (TMP/SMX) is recommended for patients with cirrhosis and ascites after initial infection. Based on spectrum of activity and side effect profile, oral third-generation cephalosporins are potential alternatives to these agents, but there are no studies examining use for this indication. The purpose of this study was to compare the recurrence of SBP infection for patients discharged on secondary SBP prophylaxis with a third-generation cephalosporin versus a fluoroquinolone or TMP/SMX.

Methods: This was a nationwide retrospective cohort study across Veterans Affairs (VA) Medical Centers. Data collected from VA Corporate Data warehouse was used to identify adult veterans with cirrhosis admitted to an inpatient acute care unit for the first episode of SBP between January 1, 2009, and December 31, 2019. The primary outcome was the recurrence of SBP infection within one year of discharge. Secondary outcomes included one-year all-cause mortality and *Clostridioides difficile* (*C. difficile*) infection. Descriptive statistics and chi-square test were used for demographic and categorical data analysis, respectively, and a Kaplan Meier curve with log-rank sum test was used to examine all-cause mortality.

Results: 1417 unique patients had an episode of SBP during the study time frame and met inclusion and exclusion criteria. 321 patients received secondary prophylaxis antibiotics with a cephalosporin (n=7), fluoroquinolone (n=266), and TMP/SMX (n=48), while the remaining population did not receive any prophylactic antibiotic on discharge (n=1096). Recurrence rates for patients who received cephalosporins (28.6%), fluoroquinolones (24.8%), and TMP/SMX (35.4%) were similar compared to those without antibiotics (30.3%, p=0.266). All-cause mortality at one year differed among patients who received cephalosporins, fluoroquinolones, TMP/SMX, and no antibiotics with mortality rates of 85.7%, 43.2%, 39.6%, and 57.1%, respectively (p<0.00001). Patients who received any antibiotic for secondary prophylaxis had a 26.5% recurrence of SBP within one year of discharge, and those who received no antibiotics had a 30.3% recurrence (p=0.187). Patients who did not receive any antibiotic had significantly higher mortality at one year (57.1%) than those who received secondary prophylaxis (43.6%, p<0.00001). There were no incidences of *C. difficile* infection during the study time frame.

Conclusions: Most veterans did not receive secondary antibiotic prophylaxis for SBP upon discharge from a VA medical center. Due to the small number of patients who received cephalosporins, it is difficult to draw meaningful conclusions for its use for this indication. Further investigation is needed to understand why secondary prophylaxis is often not prescribed after an initial SBP episode at VA facilities.