Cefpodoxime for Spontaneous Bacterial Peritonitis Prophylaxis: Incidence of Breakthrough Infections

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Background

- Spontaneous bacterial peritonitis (SBP) is a common and severe infection with high morbidity and mortality in patients with cirrhosis. The current American Association for the Study of Liver Diseases (AASLD) guidelines recommend initiating prophylaxis in three specified high-risk groups outlined in Table 1.[1,2]

Table 1: AASLD Prophylaxis Guideline Recommendations

High-risk patients	Prophylactic Agents
Prior history of SBP	**Preferred:** Oral norfloxacin daily **Alternative**: Oral ciprofloxacin daily
Cirrhosis and gastrointestinal bleeding	Ceftriaxone IV daily for 7 days
Cirrhosis and ascitic fluid protein < 1.5 g/dL, along with: • Renal dysfunction (creatinine > 1.2 mg/dL, blood urea nitrogen > 25 mg/dL, or serum sodium < 130 mEq/L) or • Liver failure (Child-Pugh score > 9 and bilirubin >3 mg/dL)	**Preferred:** Oral norfloxacin daily **Alternative:** Oral ciprofloxacin daily

- Although the guidelines only endorse the use of fluoroquinolones for oral SBP prophylaxis, many experts also use trimethoprim-sulfamethoxazole (TMP-SMZ) based on limited data. Wide-spread use of these agents, however, is associated with significant adverse reactions and the development of bacterial resistance.[2,3]
- A large proportion of patients at the Hospital of the University of Pennsylvania are initiated on cefpodoxime as SBP prophylaxis given its favorable safety profile and coverage of anticipated pathogens. However, there is no data describing its utility and/or safety. This raises the theoretical concern for increased SBP recurrence and selection of cephalosporin-resistant pathogens.
- We aim to compare its rates of breakthrough SBP to historical rates seen with TMP-SMZ and fluoroquinolones and identify the risk of cephalosporin-resistant pathogens.

Methods

Study Design:

- Single center, retrospective, cohort analysis of all patients newly started on cefpodoxime for SBP prophylaxis between March 1, 2016 and December 31, 2020
- Approved by the University of Pennsylvania Institutional Review Board

Inclusion Criteria	Exclusion Criteria
• Age ≥ 18 years old • Patients newly started on cefpodoxime at discharge for primary or secondary SBP prophylaxis	• Patients on fluoroquinolones or TMP-SMZ for SBP prophylaxis • Patients with no documentation of follow up within 12 months of therapy • Patients who received prophylaxis for gastrointestinal bleeding

Primary Outcome:

- Incidence of breakthrough SBP within 1 year of initiating cefpodoxime

Secondary Outcome:

- All-cause mortality rates within 1 year of initiating cefpodoxime
- Pathogens and susceptibility patterns isolated during the study time frame in patients with recurrent SBP

Results

Table 2: Baseline and Clinical Characteristics

	Cefpodoxime (N = 90)
Male sex – no. (%)	59 (65.6)
Age in years – mean ± SD	59 ± 13
Race – no. (%)	
White	62 (68.9)
Black	19 (21.1)
Hispanic/Latino	8 (8.9)
Asian	1 (1.1)
Other	0 (0)
Comorbidities – no. (%)	
Diabetes	40 (44.4)
Hepatocellular carcinoma	14 (15.5)
Liver transplant	7 (7.8)
Cirrhosis Etiology – no. (%)	
Alcohol-related	48 (53.3)
Non-alcoholic steatohepatitis (NASH)	24 (26.7)
Hepatitis B Virus (HBV)	4 (4.4)
Hepatitis C Virus (HCV)	24 (26.7)
Cryptogenic	7 (7.8)
Other	12 (15.6)
Mean MELD Score ± SD	20.3 ± 6.7
Serum sodium, mmol/L – mean ± SD	135 ± 5.5
Serum creatinine, mg/dL – mean ± SD	1.63 ± 1.45
Bilirubin, mg/dL – mean ± SD	4.24 ± 5.5
INR – mean ± SD	1.5 ± 0.38
CVVHD for ≥24 hours or dialysis 2x in the past week – no. (%)	9 (10)
Full year of cefpodoxime completion – no. (%)	19 (21.1)
Indication for cefpodoxime – no. (%)	
Primary prophylaxis	60 (66.7)
Secondary prophylaxis	30 (33.3)
Target cefpodoxime dose on discharge – no. (%)	79 (87.8)
Subtherapeutic dosing	6 (6.7)
Supratherapeutic dosing	2 (2.2)

Table 3: Primary and Secondary Outcomes

Primary Outcome	
Incidence of SBP within 1 year of initiation, full cohort – no. (%)	3/90 (3.3)
Incidence of SBP within 1 year of initiation, patients who completed 1 year of cefpodoxime – no. (%)	1/19 (5.2)
Secondary Outcomes	
All-cause mortality within 1 year of initiation – no. (%)	37/90 (41.1)
Ascites cultures with microbial growth – no. (%)	2/3 (66.7)

Table 4: Clinical Characteristics of Patients With Incidence of SBP

Patient	Pathogen	History of growing same organism?	Prophylaxis Indication	Duration of cefpodoxime until SBP occurrence (month)	1-year mortality?
1	*Citrobacter spp.* **Resistant to ceftriaxone**	No	Secondary	1	No
2	*Enterococcus* spp. & *C. glabrata*	No	Secondary	6	Yes
3	Negative culture	No	Primary	9	No

Limitations

- Single-centered, retrospective study with small sample size
- EMR software change in 2016 limited the ability to identify all patients admitted with cirrhosis based on ICD code
- High acuity population with advanced disease resulting in high 1-year mortality rate
- Unable to account for other courses of antimicrobials prescribed post-discharge

Conclusions

- SBP incidence observed with cefpodoxime prophylaxis was similar to historical data with non-cephalosporin prophylaxis.
  - Incidence of breakthrough SBP for patients on commonly utilized agents (TMP-SMZ vs. norfloxacin) for both primary and secondary SBP prophylaxis was about 5%.[3]
  - While the incidence of SBP in the study was low, a major concern of prolonged use of these agents is the increase of bacterial resistance.
- SBP prophylaxis with cefpodoxime appears to be a viable option to guideline-recommended non-cephalosporins with an advantageous safety profile and low rates of bacterial resistance.
- Further and larger studies are necessary to determine the utility of cefpodoxime for SBP prophylaxis, including those at different centers and in patients with less severe diseases who may be on prophylaxis for a longer time period.

References

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