SHORT REPORTS

Proton Pump Inhibitor-Associated *C. difficile* Infection in a Peritoneal Dialysis Patient

The prevalence of community-acquired *Clostridium difficile* infection (CDI) is rising and is not always associated with antibiotics (1). Renal failure is a risk factor for both contracting CDI and increased disease severity (2). Several potential risk factors for community acquired CDI are of particular importance for peritoneal dialysis (PD) patients including proton pump inhibitor (PPI) use and outpatient healthcare exposure (1). An association between CDI and PPIs has not been shown in the dialysis population specifically but is concerning given that these patients are at increased risk for gastroesophageal reflux disease (GERD), resulting in more PPI use (3). We report a case of a PD patient who developed CDI without recent antibiotic use in the setting of PPI exposure.

CASE REPORT

A 48-year-old woman with end-stage renal disease due to diabetes who had been on continuous cycling PD for 6 months presented to the hospital with a 2-day history of nausea, vomiting, abdominal bloating, watery diarrhea, and hematochezia. She had no recent antibiotic exposure. Her health care exposures were monthly dialysis clinic appointments and an endocrinology appointment 10 days prior to presentation. Two months before this episode, she was prescribed a PPI for GERD symptoms (esomeprazole initially, then switched to omeprazole).

On presentation, she was afebrile and hypertensive (178/80). Her abdomen was mildly distended. Laboratory test values were significant for a white blood cell count of 12,000/mm³ and a hemoglobin of 9.5 g/dL. Her peritoneal fluid showed 20 nucleated cells/μL and the culture was negative. A computed tomography (CT) scan of her abdomen and pelvis revealed diffuse colitis. Stool analysis confirmed the presence of *C. difficile* toxin B, but was otherwise negative. Her PPI was discontinued on admission and her symptoms slowly improved on oral vancomycin. Although the CDI was eradicated, the patient continued to have nausea, vomiting, and bloating. This was managed with prokinetic and antiemetic agents that offered partial relief. She was changed to a histamine receptor antagonist but, given her continued symptoms, she was restarted on a PPI (pantoprazole) about 3 months after discharge. Her symptoms have improved but are still present. To date, she has not had another episode of CDI.

DISCUSSION

Clostridium difficile infection is particularly important in chronic kidney disease patients as it is associated with higher mortality, increased hospital stays, and increased colectomies (2). *Clostridium difficile* infection-related diarrhea may also alter fluid and electrolyte balance, affecting PD requirements, and may predispose to peritonitis by enteric organisms (4). Our patient had CDI in the absence of antibiotic exposure. Two CDI risk factors identified were PPI use and recent outpatient appointments. In addition, PD patients may be at increased risk for CDI for several other reasons, including hypoalbuminemia (5–6) and uremic toxin-induced dysregulation of immune function (7). Furthermore, toll-like receptor 4 (TLR4) and T-cell function are important in the recognition and clearance of *C. difficile* and both are diminished in PD patients (8–10). Glucose-based PD fluids further downregulate toll-like receptors and cause peritoneal mesothelial cells to be less responsive to pathogens (11). This combination may increase both the chances of a PD patient developing CDI and translocation of *Clostridium* across the gastrointestinal wall causing *C. difficile* peritonitis (12). Proton pump inhibitors *per se*, however, have not been associated with an increased risk of peritonitis (13).

Several mechanisms have been proposed to explain the relationship between PPIs and CDI. Proton pump inhibitors increase gastric pH, which may allow for conversion of *C. difficile* spores into vegetative cells that are able to survive in the higher gastric pH (14). Further, hypochlorhydria alters the microbiota in all parts of the gut, which may affect *Clostridia* concentration and risk of CDI (15). Proton pump inhibitors also cause magnesium depletion (16), but whether this affects gut motility or subsequent CDI risk is unknown. Aside from PPI exposure, another risk factor for our patient was dialysis clinic and endocrinology appointments. Recent outpatient healthcare exposure was seen in 40% of outpatient CDI cases, highlighting the importance of hand hygiene in medical settings (1).

Alternative therapies for GERD such as pro-motility agents, anti-emetics, and/or acid suppression therapy should be tried in place of PPIs to help limit a patient's risk of CDI. Although association does not prove causality, the strong relationship between PPIs and CDI gives reason to reconsider their indiscriminate use in PD patients.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

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doi: 10.3747/pdi.2014.00057