

Antibiotic Prophylaxis in Peritoneal Dialysis Patients

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Peritonitis is an important cause of morbidity, mortality, and technique failure in patients on peritoneal dialysis (PD). The most effective approach to peritonitis is prevention, which includes careful patient training and follow-up. Although peritonitis as a result of contiguous spread of bacteria or fungi during invasive procedures, or as a result of seeding of the peritoneum during bacteremia, is uncommon, the likelihood of such spread is often predictable, and the risk can be mitigated with antibiotic prophylaxis. Here, we describe the rationale for, and approach to, antibiotic prophylaxis in PD patients for the prevention of infective episodes.

Key words

Antibiotics, peritonitis, prevention, bacteremia

Introduction

Peritonitis is the leading cause of technique failure and of patient transfer from peritoneal dialysis (PD) to hemodialysis. Not only do costs increase as a result of modality change, but significant morbidity and mortality are also associated with peritonitis (1,2). Gram-positive bacteria are responsible for most episodes of peritonitis, but gram-negative bacteria, usually enteric in origin, are associated with worse outcomes (3).

The best treatment for peritonitis is prevention. For that reason, there is growing acceptance of antibiotic prophylaxis for various procedures that could lead to bacterial flux into the peritoneal cavity. Here, we summarize the recent literature to provide guidance about the use of prophylactic antibiotics in PD patients undergoing procedures. Furthermore, we outline the evidence for prophylaxis against fungi in PD patients who are receiving antibiotics.

Discussion

Endoscopy in PD patients

Several studies have looked at PD patients undergoing colonoscopy. Yip *et al.* (4) reported on 97 colonoscopies performed in 77 patients, observing a 6.3% rate of peritonitis after colonoscopy. Patients who were given prophylactic antibiotics did not develop colonoscopy-related peritonitis. The authors also noted that no increase in the rate of peritonitis was observed in patients who underwent polypectomy. Wu *et al.* (5) reported a similar post-endoscopy peritonitis rate of 6.4% and noted that no patient prescribed prophylactic antibiotics developed peritonitis. In addition, several other small case reports demonstrated the phenomenon of peritonitis after colonoscopy, with some even reporting a much higher rate of peritonitis (increased by a factor of 3 – 5) in patients undergoing polypectomy than in those having nontherapeutic colonoscopy (5–9).

The guidelines from the International Society for Peritoneal Dialysis (ISPD) recommend prophylactic antibiotics before colonoscopy. They suggest using 1 g ampicillin, plus a single dose of an aminoglycoside, with or without metronidazole, given intravenously or intraperitoneally; further, the abdomen should be drained before the procedure (10,11). That recommendation is mirrored in a guideline paper published in 2015 by the American Society of Gastrointestinal Endoscopy (12).

The pathogenesis of peritonitis after colonoscopy has been hypothesized to be secondary to translocation of bacteria to the portal circulation, followed by seeding of the peritoneal cavity (13). Another more likely hypothesis is translocation across the bowel wall through tears and microperforations caused by colonoscopy and insufflation of the bowel during the procedure (14). Although bacterial seeding of the peritoneal cavity likely occurs in most patients during colonoscopy, PD patients are disadvantaged because of the unphysiologic composition of dialysate, including its high glucose

content and low pH. Those characteristics lead to impaired phagocyte function and thus increase the risk of infection (15).

Like colonoscopy, esophagogastroduodenoscopy (EGD) has also, in case reports, been linked to bacteremia and peritonitis in PD patients (5,16–18). The rate of EGD-related peritonitis has been noted in one study to be approximately 8%, with rates increasing to upward of 20% during sclerotherapy of varices, esophageal dilation, and instrumentation of obstructed bile ducts (12,19,20). In a study by Wu *et al.* (5), it was further observed that no peritonitis occurred in the group of PD patients who were prescribed prophylactic antibiotics; however, that result was not statistically significant. Unlike the situation for colonoscopy, the ISPD guidelines do not specifically mention provision of prophylactic antibiotics in patients undergoing EGD.

Other procedures in PD patients

Morimoto *et al.* (16) and Ma *et al.* (21) both reported peritonitis in a PD patient after a gynecologic procedure. The patient in Morimoto's paper developed peritonitis after two separate gynecologic examinations for vaginal bleeding. Ma and colleagues described a patient who developed peritonitis after cervical conization and endocervical curettage. Both authors also noted that neither patient developed gynecologic procedure-related peritonitis when prophylactic antibiotics were used before subsequent procedures. Other reports have noted a peritonitis rate as high as 38% after these kinds of procedures (5,22). The ISPD guidelines acknowledge the association and recommend prophylactic antibiotics before invasive gynecologic procedures (10).

Dental work has likewise been associated with both bacteremia and peritonitis in PD patients. Kiddy *et al.* (23) reported on 4 patients who developed *Streptococcus viridans*-related peritonitis after dental procedures for oral lesions, including dental filling, boil on gum, bleeding lesion on gum, and traumatic abrasion of the lip. Shukla *et al.* (24), Levy *et al.* (25), and Fried *et al.* (22), all described cases of *Streptococcus viridans* peritonitis after dental procedures, with Levy *et al.* focusing on the pediatric patient population. The ISPD guidelines thus recommend that a single dose of amoxicillin be provided before dental procedures, as described in earlier recommendations for endocarditis prophylaxis (10).

Fungal prophylaxis

Fungal peritonitis in PD patients, although rare, is a serious and often life-threatening complication, with mortality rates ranging between 17% and 44% (26–30). Risk factors that predispose to fungal peritonitis remain unclear; however, recent antibiotic use has been noted in several studies to play an important role. For example, Eisenberg *et al.* (27) note that 69% of patients with fungal peritonitis had received antibiotics within the preceding month. Goldie *et al.* (31) similarly noted that 75% of patients with fungal peritonitis had received antibiotics within the preceding 3 months. One of the reasons postulated for the relationship with antibiotic use is that such use increases gut yeast colonization, which leads to fungal peritonitis. However, publications from authors such as Thodis *et al.* (30) and Lo *et al.* (32) refute the relationship and report no association between antibiotic use and the incidence of fungal peritonitis. Nonetheless, because of the possible relationship between recent antibiotic use and the incidence of fungal peritonitis, there has been much interest in prophylaxis with nystatin or fluconazole during a course of antibiotics.

Several retrospective and prospective studies have debated the utility of antifungal prophylaxis in PD patients taking a course of antibiotics (30,33–36). The Pan-Thames study (37) reported on 49 cases of fungal peritonitis in 3322 peritonitis episodes and observed a statistically nonsignificant decrease in the number of fungal peritonitis episodes in patients receiving fluconazole prophylaxis compared with patients not receiving such prophylaxis. To date, two prospective randomized controlled trials have been published on the topic: one by Lo *et al.* (32) and the other by Restrepo *et al.* (38). The former study, published in 1996, looked at 397 PD patients randomized to either control or prophylaxis using 500,000 U nystatin 4 times daily whenever antibiotics were prescribed. Compared with the control group, the group receiving prophylaxis had a significant higher probability of *Candida* peritonitis-free survival (0.974 vs. 0.915, $p < 0.05$). However, as mentioned earlier, the incidence of *Candida* peritonitis in patients using antibiotics was not observed to be statistically significantly increased (32). The trial by Restrepo *et al.*, published in 2010, assessed the use of prophylactic fluconazole in patients prescribed antibiotics for peritonitis, exit-site infection, or tunnel infection. That study also noted a statistically significant decrease in the rate of

fungal peritonitis in the group receiving prophylaxis compared with the control group (0.92% vs. 6.45%, $p = 0.0051$).

The 2016 guidelines from the ISPD now recommend the use of antifungal prophylaxis in PD patients who receive a course of antibiotics. They suggest that either nystatin or fluconazole can be used; however, they also include cautions about side effects and drug interactions with the use of fluconazole (10).

Summary

Given the high rates of mortality and morbidity associated with peritonitis, it is imperative that prevention always be a primary concern. Providing antibiotic prophylaxis to patients undergoing colonoscopy, invasive gynecologic procedures, dental procedures, and EGD has been shown to reduce the peritonitis rate in PD patients. Furthermore, fungal prophylaxis with either nystatin or fluconazole is also strongly recommended for patients receiving a course of antibiotics.

Disclosures

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