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Narrative Review

Peritoneal Dialysis–Related Peritonitis: Towards Improving Evidence, Practices, and Outcomes

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Peritonitis is a common serious complication of peritoneal dialysis that results in considerable morbidity, mortality, and health care costs. It also significantly limits the use of this important dialysis modality. Despite its importance as a patient safety issue, peritonitis practices and outcomes vary markedly and unacceptably among different centers, regions, and countries. This article reviews peritonitis risk factors, diagnosis, treatment, and prevention, particularly focusing on potential drivers of variable practices and outcomes, controversial or unresolved areas, and promising avenues warranting further research. Potential strategies for augmenting the existing limited evidence base and reducing the gap between evidence-based best practice and actual practice also are discussed.

INDEX WORDS: Antibiotics; bacteria; fungi; microbiology; outcomes; peritoneal dialysis; peritonitis; practice variation; prevention; quality improvement; risk factors.

David W. Johnson, PhD, was an International Distinguished Medal recipient at the 2014 National Kidney Foundation Spring Clinical Meetings. The International Distinguished Medals are awarded to honor the achievement of individuals who have made significant contributions to the field of kidney disease and extended the goals of the National Kidney Foundation.

Peritoneal dialysis (PD) is used to treat end-stage kidney disease in more than 200,000 patients across 130 countries worldwide and accounts for ~11% of the global dialysis population.[1,2] Its outcomes are comparable to those of hemodialysis and may even be superior in the first few years.[3,4]

One of the most serious complications of PD is peritonitis, which results in considerable morbidity and mortality. PD peritonitis directly contributes to ~20% of PD technique failures[5] and 2%-6% of deaths.[6,7] Severe and/or persistent peritonitis also may lead to peritoneal membrane failure and possibly to encapsulating peritoneal sclerosis.[8-10] This article reviews the epidemiology, risk factors, diagnosis, treatment, and prevention of PD peritonitis, particularly focusing on controversial or unresolved areas or promising avenues warranting further research. Potential strategies to reduce the observed high variability in practices and outcomes among different PD units also are discussed.

EPIDEMIOLOGY

There is wide variation in rates of PD peritonitis across different centers and countries. Reported rates range from 0.06-1.66 episodes/patient-year.[11] These reports tend to be dominated by single-center studies, which may reflect publication bias because overall peritonitis rates tend to be higher in unselected multicenter studies.[12,13] Even within the same country, peritonitis rates vary substantially among PD units. In a previous analysis of data from the Australian and New Zealand Dialysis and Transplant Registry (ANZDATA) in 2003-2008, our group demonstrated a 10-fold variation in PD peritonitis rates among centers that was not related to center size.[12] Three years later, the magnitude of this variation still is considerable and is not explained by differences in center size or case-mix (Fig 1). Similarly, Kavanagh et al[14] demonstrated almost 5-fold variation in peritonitis rates (0.78-3.8 episodes/patient-year) in a study of 10 adult renal units in Scotland between 1999 and 2002. Interunit differences in peritonitis rates were not explained by center size, number of PD patients per nurse, or average PD training time, although peritonitis rates (particularly due to *Staphylococcus aureus*) were lower in units using nasal mupirocin.[14] Comparable results (7-fold variation) also were reported in a study of 12 PD units in the Thames area of the United Kingdom.[13]

Although some of these observed differences may be related to different approaches to patient selection

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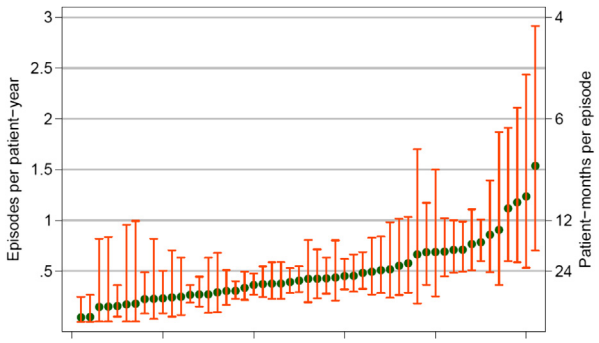

Figure 1. Peritoneal dialysis (PD) peritonitis rates by treating center in Australia and New Zealand in 2011. Confidence intervals are not shown when upper limit is >3. Units with fewer than 5 person-years of PD over 2011 are not shown. Reproduced with permission from the ANZDATA 2012 Annual Report.[5]

or assessing peritonitis episodes, it is likely that practice variation was a major driver of outcome differences. For example, a nationwide survey of 23 Austrian PD centers demonstrated that infection prophylaxis strategies and PD-associated infection rates varied widely by center.[15] Importantly, the authors identified lower mean infection rates in units performing prophylactic mupirocin therapy in *S aureus* carriers, although they did not formally statistically analyze the data.[15]

Overall, peritonitis rates generally have been reported to be decreasing over time. A retrospective observational cohort study of a single PD center in Korea[16] reported significant improvement in peritonitis rates from 0.57 episodes/patient-year in 1993 to 0.29 episodes/patient-year in 2005. However, the improvement occurred primarily in Gram-positive peritonitis, whereas Gram-negative peritonitis rates were constant. The change in peritonitis pattern was attributed to improvements in PD equipment, leading to a reduction in contamination with skin organisms during connection procedures. Similar findings were reported by single-center studies in Brazil,[17] Portugal,[18] and Taiwan.[19] Although the introduction of twin-bag connection systems was a major contributor to reductions in peritonitis rates,[7,20] other factors include better identification of peritonitis risk factors,[7] introduction of mupirocin prophylaxis for *S aureus* carriers,[21] application of gentamicin cream to exit sites,[22] and fluconazole or nystatin prophylaxis for fungal peritonitis.[23]

RISK FACTORS

Reported risk factors for PD peritonitis are listed in Box 1. The majority of these associations originate from outcomes based on observational studies and may relate to factors that increase the risk of infection generally (eg, diabetes mellitus,[12,24] frailty, and comorbid disease burden[24-26]) or of peritonitis specifically (eg, positive nasal *S aureus* carrier status[27] and history of exit-site infection[28,29]). Furthermore, there are several demographic factors that have been associated inconsistently with increased risk of peritonitis, such as age,[24,30] sex,[30-32] and ethnicity.[5,11,12,24-26,33,34] To date, there are conflicting reports regarding the impact of biocompatible fluids[35-49] and automated PD (APD)[19,30,50,51] on peritonitis rates, such that currently, no conclusions can be drawn about these interventions.

Box 1. Reported Risk Factors for PD Peritonitis

Non-modifiable

- Older age[24,30]
- Female sex[30-32]
- Indigenous racial origin[a,12,24-26,33]
- Black ethnicity[34]
- Lower socioeconomic status[115,116]
- Diabetes mellitus[12,24]
- Coronary artery disease[24,26]
- Chronic lung disease[24]
- Hypertension[25]
- Poor residual kidney function[117]

Modifiable

- Obesity[12,24,25]
- Smoking[24]
- Living distantly from PD unit [26,118]
- Depression[119,120]
- Hypoalbuminemia[34,121]
- Hypokalemia[122]
- Medical procedures (eg, colonoscopy)[123]
- Absence of vitamin D supplementation[124]
- Biocompatible fluids[b,41]
- Nasal *Staphylococcus aureus* carrier status[27]
- Previous exit-site infection[28,29]
- PD against patient's choice[51,125]
- Prior hemodialysis[126]
- Pets[127]
- Patient training[104,106,128]

Abbreviation: PD, peritoneal dialysis.

[a]Indigenous racial origin includes Aboriginal and Torres Strait Islander, Maori and Pacific Islander, and First Nation Canadian racial origin.

[b]Reduced peritonitis risk with the use of biocompatible fluids is not consistently supported.[107,129]

In addition to these variables, some risk factors may be associated with organism-specific peritonitis episodes only rather than overall peritonitis risk. For example, peaks in the incidence of peritonitis due to coagulase-negative staphylococci and Gram-negative organisms in warmer seasons and *Corynebacterium* species in winter demonstrate seasonal variations in organism-specific peritonitis rates.[52] These variations have been attributed to both climate-related changes in human behavior and immunity, as well as variable organism virulence.[52] Similarly, recent antibiotic therapy and recent peritonitis also have been identified as risk factors for fungal peritonitis.[53]

Although a number of the reported risk factors for PD peritonitis listed in Box 1 are modifiable, there currently is no high-level evidence that modifying