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Prevention and management of peritoneal dialysis associated infections in children: Continuing to grow and reaching new milestones

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The prevalence and types of kidney replacement therapy for children with end-stage kidney disease (ESKD) vary widely, with a global prevalence of 18 to 100 per million age-related population, of whom approximately 25% are on dialysis.[1] Peritoneal dialysis (PD) is the dialysis modality of choice for children in most parts of the world. Advances in technology have improved outcomes even for the youngest children, but infectious complications such as peritonitis have a reported pediatric incidence of nearly 0.41 episodes/patient-year, leading to an increase in morbidity and hospitalization rates, potential modality change to hemodialysis, and increased mortality.[2,3] However, incidence and prevalence vary considerably across countries and regions, and consensus guidelines can assist providers in the prevention, treatment, and monitoring of patients. Catheter-related infections pose a significant threat to patient safety, and analysis of risk factors, exit site treatment, and optimization of antimicrobial treatment highlight critical areas for intervention.[4]

The clinical practice guidelines (CPG) by Warady et al. provide a comprehensive overview of the prevention and treatment of peritonitis, through a systematic review of the existing literature, accompanying grading, and risk of bias analyses. These consensus guidelines provide a significant improvement on the group's 2012 guidelines by including a focus on quality improvement programs and clinical training of healthcare providers and caregivers drawing on expertise from the Standardizing Care to Improve Outcomes in Pediatric End Stage Renal Disease (SCOPE) Collaborative.[5] Also, for the first time, the International Society for Peritoneal Dialysis (ISPD) guidelines pay careful attention to antibiotic stewardship advocating treatment for the shortest effective duration where safely possible. The authors have identified and constructed 54 patient/population, intervention, comparison, and outcomes (PICO) questions to address all aspects of PD-related infection management.

A rigorous methodology is used, and in this field with low-level evidence in many areas, pragmatic guidance rather than a default position of therapeutic nihilism has been adopted. These updated recommendations address specific aspects of antibiotic prophylaxis at PD catheter placement, exit site care, non-antimicrobial treatment to prevent peritonitis, and the treatment of peritonitis in patients receiving PD. Several key aspects are discussed below.

Infections related to catheter placement can significantly impact patient morbidity and contribute to peritonitis and technique failure. The CPG by Warady et al. recommends the utilization of a double-cuff Tenchkoff catheter, individualized PD catheter placement, and perioperative intravenous antibiotic treatment to reduce infection risk among pediatric patients. A systematic review conducted by Htay et al.[6] in 2019 reported no major evidence supporting the claim that various catheter modalities or insertion methods decreased PD infection risks, but their analysis was limited by the sample size and quality of the studies. A new section in the 2024 guidelines is on antibiotic prophylaxis at the time of PD catheter insertion. Prophylactic antibiotics together with meticulous exit site care are important processes in reducing infection risk and supporting healing. The guidelines provide a conditional recommendation to postpone the initial PD catheter dressing change for at least seven days after catheter insertion, while promptly removing soiled, loose, or damp dressings. This reflects other consensus reviews regarding catheter-related infections, which also recommend prophylactic antibiotic administration and

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maintaining clean exit site dressings for 1 week to allow for catheter immobilization and decreased infection risk.[7] The CPG by Warady et al. provides epidemiological data alongside diagnostic protocols and long-term treatment. Reassuringly, a 5-year retrospective analysis of adult PD patients reported a significant decrease in catheter-associated infections while maintaining comparable antibiotic resistance patterns with consistent monitoring, exit site care, and treatment.[8]

Patients with a stoma are at an inherently greater risk of peritonitis, requiring targeted antibiotic (and in some cases antifungal) prophylaxis. The placement of gastrostomy feeding tubes that are frequently needed in young children with ESKD must be carefully planned, ideally before starting PD. There are conflicting data on the risk of peritonitis with gastrostomy tube placement techniques, with most authors promoting open rather than laparoscopic gastrostomy placement in children on PD; these potential discrepancies are extensively discussed within the recommendations and associated rationale.[9–13]

Recommendations on the diagnosis and treatment of complex and recurrent peritonitis are also presented, affirming the importance of antibiotic stewardship with dosing strategies to minimize antibiotic resistance.[14,15] The minimum effective time of treatment to reduce both antibiotic resistance and re-infection risk is extensively discussed. A meta-analysis by Mo et al.[16] reported that decreased antibiotic treatment duration was associated with a reduction in antibiotic resistance, and a retrospective cohort analysis of hospitalized adult patients by Brower et al.[17] further affirmed that most patients were treated with antibiotics beyond recommended guidelines. By reducing unnecessary and/or prolonged antibiotic interventions and promoting individualized therapy, patients have decreased risk of fungal or other opportunistic infections and improved antibiotic stewardship. However, the shorter treatment duration of only 2 weeks even for virulent organisms such as *Staphylococcus aureus* and several gram-negative organisms, differs from the organism-specific treatment recommendations in the adult ISPD guidelines and is based on low-certainty evidence derived predominantly from the International Pediatric Peritoneal Dialysis Network (IPPN) registry.

In fact, there is no primary literature cited to support the three-week duration of therapy recommended for gram-negative peritonitis (albeit with notable exceptions for organisms including *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and species, and *Stenotrophomonas maltophilia*) even within the adult ISPD guidelines, and there was no evidence to support this recommendation within the pediatric guidelines from 2012 either. Notably, the recommendation for 3 weeks of antibiotic treatment for gram-negative peritonitis in adult PD patients is based on two retrospective observational studies performed over two decades ago. For the current guidelines, the authors justify a shorter antibiotic treatment course based on a rigorous analysis of the IPPN registry data on the treatment and outcomes of gram-negative peritonitis in nearly 300 children, fully acknowledging the limitations of registry data. Although these data are yet to be published, the authors report that there was no difference in outcomes in children receiving two versus three weeks of antibiotics.

Modifications of treatment for peritonitis variants are also addressed within the guidelines, tailoring care for differing patient presentations. Recommendations are provided for mycobacterial, fungal, culture-negative, gram-positive, and gram-negative peritonitis, describing comparative patient outcomes, disease etiologies, and varied treatment rationales for each condition. A retrospective cohort study of 888 pediatric PD patients by Kamath et al.[2] reported an incidence of 45.9% for gram-positive peritonitis, 26.4% for gram-negative, and relatively uncommon mycobacterial and fungal peritonitis cases, with a significantly higher peritonitis rate in centers with a shorter duration of training.

Peritonitis relapses also pose a significant threat to patient health, with increased mortality and technique failure and decreased cure rates compared to primary incidence.[18]

The guideline also provides several recommendations discussing continuing treatment, follow-up diagnosis, and catheter removal, allowing for longitudinal assessment and prevention of further infection.[19] The breadth of the rationale discussing therapy modifications, individual patient treatment objectives, and potential confounding factors builds upon existing epidemiological and clinical research and allows physicians a standardized approach, which one hopes will support improved outcomes.

There are significant differences in clinical treatment and diagnosis between pediatric and adult PD patients, and the CPG by Warady et al. addresses discrepancies between clinical recommendations from the ISPD for pediatric and adult guidelines together with a detailed rationale. Acknowledging the limitations associated with the adult implementation of dialysis care is especially important when considering the variations in dialysis utilization among pediatric and adult patients. Nearly 45% of pediatric dialysis patients within the United States receive PD treatment as compared to below 17% of adult kidney failure patients, demonstrating the unique importance of pediatric literature and research in PD treatment outcomes.[20] Furthermore, pediatric patients have additional aspects of care including attention to appropriate electrolyte balance, fluid management, and promoting optimal growth requirements, necessitating careful monitoring and tailored treatment.[21]

Despite the detailed recommendations and systematic review conducted by Warady et al., there are some limitations that must be considered. First, due to the heterogeneity of the studies included in the systematic review, no quantitative statistical analysis was performed to support the established recommendations, preventing statistically significant conclusions.

Moreover, the study's exclusion criteria removed publications only involving the adult population, potentially reducing the validity of conclusions regarding treatment

methods and long-term patient outcomes. The guidelines may not be generalizable across demographic, socioeconomic, and geographic regions.

The use of unpublished data from the IPPN and data from SCOPE networks to support recommendations presents concerns regarding the quality and validity of some research materials. Furthermore, while Warady et al. do analyze risk factors for peritonitis and other infections in PD patients, some uncommon conditions such as atrial septal defects and pancreatitis that are identified as risk factors for peritonitis were not described within the guidelines.[19,22] However, the comprehensive systematic review, expert review panel, and harmonization of pediatric and adult literature presented in the guidelines allow clinicians to make better-informed patient care decisions. Of the 54 PICO questions addressed, only guideline 5.1 on connectology (flush before fill) is a strong recommendation based on high certainty of evidence from seven trials in adult continuous ambulatory PD patients, while one randomized controlled trial (RCT) in 121 pediatric automated PD patients did not demonstrate a reduction in peritonitis rate.[23] Guideline 20.9. on catheter removal if a catheter-related infection progresses to or occurs in conjunction with peritonitis due to the same organism, is a strong recommendation, but based on low certainty of evidence. All other guidelines are classified as good practice statements/not graded or as conditional recommendations, based on low or very low certainty of evidence. The authors are to be congratulated for the rigorous literature search and their meticulous and transparent evidence-to-decision process. The low-level evidence underpinning the guidelines despite decades of scientific efforts is not surprising in this rare disease treatment setting where large-scale RCTs are not feasible.

Monitoring of the CPG use and resulting outcome is required, for example, in large-scale international registries such as the IPPN.

Overall, Warady et al.'s cardiopulmonary resuscitation provides an invaluable resource that will assist physicians and other healthcare professionals in the prevention and management of peritonitis and related infectious complications in pediatric PD patients.

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RR and RS: conceptualization; SS, RR, and RS: drafting; SS, RR, RS: writing; RS, CS, and RR: revision and editing.

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