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REVIEW

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Clinical practice guidelines for pediatric peritoneal dialysis

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Abstract Peritoneal dialysis (PD) continues to be an important modality of treatment for children with end-stage renal disease. The Canadian Association of Pediatric Nephrologists recognized the need nationally to review the literature on the delivery of PD in children to provide optimal standardized care. This resulted in the development of the Canadian Clinical Practice Guidelines for pediatric PD. Clinical practice guidelines are a useful adjunct to clinical care. The present review includes recommendations for catheter placement and types, requirement for prophylactic omentectomy, initiation and adequacy of dialysis, PD prescription, and solute clearance. It provides physicians with updated evidence-based recommendations that include consideration towards practicality with the major goal of improved and standardized patient care.

Keywords Guidelines · Peritoneal dialysis · Children · Canadian · Evidence-based practice

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Introduction

The importance of peritoneal dialysis (PD) to the delivery of chronic renal replacement therapy in children in North America is underscored by the latest data released by the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) [1]. PD in the 2004 NAPRTCS annual report is the initial modality chosen in 60% of children started on dialysis and is currently used to dialyze 65% of children within Canada and North America [1, 2].

With the publication of the National Kidney Foundation Dialysis Outcome Quality Initiative (NKF K/DOQI) and the Clinical Practice Guidelines by the Canadian Society of Nephrology (CSN), the Canadian Association of Pediatric Nephrologists (CAPN) recognized a need for the development of similar guidelines specific to the care of children on dialysis [3–5]. The Ad Hoc European Committee has published several reviews on pediatric peritoneal dialysis but there are some aspects of care across continents that are different [6–8]. A brief survey of present pediatric peritoneal dialysis practices within Canada demonstrated variability of care across the country. The aim of the Canadian Pediatric Peritoneal Dialysis group was to develop best evidence-based guidelines for pediatric peritoneal dialysis by utilizing the available pediatric, and where significant, the best of the adult literature, with the hope of achieving uniform evidence-based standards for Canadian children on peritoneal dialysis.

Materials and methods

CAPN set up a working group of practicing pediatric nephrologists to comprehensively review different aspects of pediatric peritoneal dialysis with the goal to provide evidence-based recommendations within specific areas. The focus of the review was limited to addressing technical and adequacy issues of PD in children and did not address non-dialysis issues such as renal osteodystrophy, anemia, nutritional issues, growth, and/or acid-base problems.

The following guidelines outline the best evidence available to craft recommendations in children; however, most are not supported by robust evidence from the pediatric literature. In areas where little or no pediatric evidence exists, where the pediatric studies are of poor quality or conversely the adult studies are outstanding, reference will also be made to the adult literature. For each guideline, the final recommendation will highlight the highest level of both pediatric and adult evidence reviewed to provide support for the recommendations made.

The grading of levels of evidence is derived from Dr. D. H. Sackett [9] and is included for all references cited and recommendations. This is the same grading system utilized on the practice guidelines of the CSN [4] (Table 1).

Guideline I: timing of initiation of peritoneal dialysis

There has been much controversy in the adult literature about timing for initiation of dialysis and whether patients would benefit from early initiation when the creatinine clearance (CrCl) is >15 ml/min per 1.73 m^2. In pediatrics, there is no clear evidence regarding the optimal time to initiate dialysis with no available studies to support any recommendations. Recent adult studies have failed to confirm any significant benefits of early initiation of dialysis [10–12]. However, it is generally accepted that dialysis should be initiated when CrCl is less than or equal to 10 ml/min per 1.73 m^2 and/or when there are symptoms and signs of uremia (i.e., nausea and vomiting, anorexia, weight loss, lethargy, poor school performance etc.).

Recommendation Peritoneal dialysis in children should be initiated when CrCl is <10 ml/min per 1.73 m^2 and/or when there are symptoms and signs of uremia and/or growth failure (opinion).

Guideline II: peritoneal catheter types

The latest NAPRTCS 2004 annual report states that Tenckhoff catheters are used in 91% of all index cases of pediatric peritoneal dialysis [1]. Similar results are reported from other countries, including Japan and Italy [13, 14]. A small pediatric study comparing the Toronto Western Hospital (TWH) catheter with the Tenckhoff catheter did suggest a possible advantage of the TWH catheter with respect to one-way obstructions (45 versus 7%, $p<0.05$) [15] (level V). However, the numbers were small and only 50% of the TWH catheter group had the catheter placed as the initial PD catheter. There is, therefore, little evidence to suggest that one catheter is superior to another.

Recommendation The use of a Tenckhoff-type catheter in all ages of pediatric patients on PD is recommended and is the standard of practice in North America (best available evidence: pediatric V).

Guideline III: number of cuffs

Use of double-cuff catheters (DCC) in pediatric patients is recommended by both the International Society of Peritoneal Dialysis (ISPD) and the Ad Hoc European Committee [7, 16]. In addition, the Ad Hoc European Committee recommends the use of a single-cuff catheter (SCC) in infants less than 3 kg (opinion based). Both recommendations are based on the 1995 NAPRTCS annual report on PD and peritonitis outcomes [17] (level V). The evidence to support these recommendations is poor with most of the pediatric studies showing no difference in peritonitis, exit-site infection rates, or leaks between DCC and SCC [18–20] (levels III and V). Conversely there are three pediatric

Table 1 Levels of grading of evidence [9]

Levels of grading	Description
I	Randomized, controlled trial (RCT) that demonstrates a statistically significant difference in at least one important outcome (i.e., survival, major illness); or if the difference is not statistically significant, a RCT of adequate sample size to exclude a 25% difference in relative risk with 80% power, given the observed results
II	A RCT that does not meet level I criteria
III	A nonrandomized trial with contemporous controls selected by some systematic method or subgroup analysis of a randomized trial
IV	A case series (at least 10 patients) without controls
V	A case series (fewer than 10 patients) without controls

reports suggesting that extrusion of the second cuff with DCC is more problematic when compared with SCC [21–23] (levels IV and V). However, the short distance of the second cuff from the exit site in these papers (<0.5 cm) would not be accepted today as an appropriate distance (~2 cm cuff to exit site). Other than this anecdotal evidence there is no evidence to suggest any disadvantage to DCC vs SCC in any other regard. No adult studies provide any higher grades of evidence to address this question. The other issue of a recommended maximal distance between the external cuff and the superficial surface is not well addressed in the literature other than by recommendations from review articles without any substantial evidence [16].

Recommendation Double-cuff catheters can be used in children heavier than 3 kg where the external cuff can be placed 2–3 cm from the exit site (best available evidence: pediatric III).

Guideline IV: exit-site direction

The use of downward oriented exit sites in pediatric patients is recommended by both the ISPD and the Ad Hoc European Committee [7, 16]. This is based again on a review of NAPRTCS data showing that a downward exit site provided significant advantage over an upward facing site in terms of the overall peritonitis rate (1 in 18.9 vs 1 in 10.6 patient months at risk, p=0.01) [17] (level V). A pediatric study by Sojo et al. compared 85 Tenckhoff straight catheters with lateral exit sites to 33 Swan neck curled catheters with downward exit sites. They were unable to demonstrate any advantage of one exit-site orientation over the other in terms of rates of peritonitis, risk of exit-site or tunnel infection, or risk of leaking [20] (III). Adult studies, the best of which is only level IV, show little evidence to either support or refute the recommendation of downward oriented sites. Nevertheless, there does not seem to be any evidence that a downward exit site predisposes to any complications.

Recommendation Exit sites should be oriented either downward (preferred) or laterally in children (best available evidence: pediatric III, adult IV).

Guideline V: subcutaneous tunnel: straight versus preformed curve (swan neck)

The use of swan neck versus straight catheters in pediatrics is briefly reviewed by Gokal et al., but there are no specific recommendations for children [16]. Based on 2004 NAPRTCS data, swan neck catheters are less commonly utilized in children as compared to catheters with a straight subcutaneous tunnel (21 vs 74%, respectively) [1]. The Ad Hoc European Committee recommends a swan neck design based on aggregate NAPRTCS data, but there are few studies that compare the two in children [7]. Sojo et al. and Jones et al. reported their results in children comparing swan neck DCC with straight subcutaneous tunnel SCC Tenckhoff catheters [20, 24]. Both groups found no significant differences between the straight subcutaneous vs swan neck tunnel with regards to peritonitis rates or exit-site infections (opinion). Adult studies by Lye et al. [25] and Eklund et al. [26] show conflicting level I and II evidence, respectively, that swan neck catheters lower the risk of exit-site infections but are in agreement with respect to their equivalency in terms of episodes of peritonitis, catheter survival, and rates of peritonitis, while Bockurt et al. present moderately strong evidence that they may reduce tip migration (level III) [25–27]. However, there is no strong evidence in children supporting swan neck over straight intramural tunnels.

Recommendation As there is no strong evidence in either the pediatric or adult literature, use of a swan neck catheter in children should be left to the discretion of the individual PD center (best available evidence: pediatric III, adult I and II).

Guideline VI: intraperitoneal segment: curled versus straight

Current 2004 NAPRTCS data show that 63% of PD catheters in children have curled intraperitoneal segments and as a percent of Tenckhoff catheters, in particular, curled segments make up almost 69% of catheters inserted [1]. Curled intraperitoneal segments also predominate in Europe although the actual numbers are not provided [28]. Recommendations from both the ISPD and the Ad Hoc Group advocate for the use of curled rather than straight intraperitoneal segments based on observations that curled intraperitoneal segments reduce the risk of mechanical failure and minimize the incidence of inflow pain and catheter tip irritation of the bowel [7, 16]. This is supported in pediatrics in a study by Lerner et al. who found a significant difference in the risk of obstruction with a straight intraperitoneal segment versus the curled catheter (12 vs 6%, respectively, p<0.05) [19] (level IV). However, in a study by Sojo et al., they did not find any significant difference in the risk of tip migration or omental capture between the straight and curled intraperitoneal segments (944 catheter months at risk for the straight peritoneal segment vs 266 months at risk for the curled segment) [20] (III). Neither of these studies showed any difference in surgical revision rates or risk of peritonitis when comparing the two intraperitoneal catheter designs. There are three randomized clinical trials in the adult literature comparing curled with straight intraperitoneal catheters [29–31] (levels I and II). One trial was terminated early because of vastly improved catheter survival with the curled intraperitoneal segment [29]. Al-Hilali's study had opposite results in a level I trial comparing immediate postoperative drainage failures due to malposition or omental wrap in curled versus straight catheters. This trial was also terminated early at a planned interim analysis after 24 patients because of the vastly superior results in the straight catheter arm [31]. Although the pediatric literature is not strong in providing evidence for or against the use of curled intraperitoneal segments, there is strong level I and II evidence in the adult population which suggests that curled segment catheters have improved survival rates and minimizes the risk of catheter tip migration.

Recommendation Children should have a PD catheter which has a curled intraperitoneal segment (best available evidence: pediatric III, adult I and II).

Guideline VII: catheter tip placement

Catheter tip placement plays a pivotal role in effluent drainage where there should be easy inflow and outflow of peritoneal dialysate fluid. The ISPD adult guidelines recommend that the catheter tip be placed between the parietal and visceral epithelium, aimed towards the pouch of Douglas and away from loops of bowel or omentum [16]. Although this premise is accepted by all nephrologists, there is a paucity of evidence to support this recommendation.

Recommendation The tip of the PD catheter should be placed, whenever possible, in the pelvis (opinion).

Guideline VIII: prophylactic omentectomy

The need for prophylactic omentectomy at the time of the PD catheter insertion remains controversial in both the adult and pediatric PD literature [32]. The opinions range between all infants and children requiring prophylactic omentectomies to that of the fact that an omentectomy should only occur when problems arise [33, 34]. In fact, only 53% (9/17) of centers in the Pediatric Peritoneal Dialysis Study Consortium when surveyed said they routinely performed omentectomies [34]. However, as catheter obstructions, most commonly due to omental and fimbrial adhesions, are second only to peritonitis in terms of major catheter complications, with rates varying between 6 and 31% [35–43], the possible importance of omentectomy in preventing this problem should not be overlooked. Children in particular may be at higher risk of omental obstruction, and although subtotal omentectomies may cause significant bleeding and trauma, performing them at initial insertion may prevent the need for a second operation to correct an omental obstruction [44]. There are few prospective and no randomized trials addressing issues related to omentectomy. There are no well-designed studies in the pediatric literature to either support or refute the use of prophylactic omentectomies as a strategy for maximizing catheter life and minimizing outflow obstruction [44, 45] (levels IV and V). The adult literature provides more robust evidence in favor of omentectomies [46–48] with one prospective study providing level III evidence [46].

Recommendation The decision to perform an omentectomy (or omentopexy if a laparoscopic insertion is contemplated) in a pediatric patient should be left to the discretion of the surgeon, bearing in mind that there is some adult evidence which suggests improved catheter survival in adults following such a procedure (best available evidence: pediatric IV, adult III).

Guideline IX: catheter insertion and the use of prophylactic antibiotics

The ISPD defers all pediatric perioperative catheter care issues, including prophylactic antibiotics, to the adult recommendations [16]. The European Ad Hoc Committee recommends a cephalosporin antibiotic be given at the time of the catheter insertion although no reference was given to support this guideline [7]. In pediatrics, Sardegna et al. addresses the issue of prophylactic antibiotics for PD catheter insertions [49] (level IV). This paper reviewed 77 SCC straight catheters inserted over a 6-year period and compared 66 insertions which received prophylactic antibiotics with 16 insertions which did not. Antibiotic prophylaxis included cefazolin and vancomycin as single agents or a combination of ampicillin and gentamicin. In the prophylactic antibiotic group, only 6 of 61 developed peritonitis as compared to 7 of 16 in the nontreated group ($p<0.001$). The reduced incidence of peritonitis was not specific to any class of antibiotic used. In the adult population, there are three level I trials clearly demonstrating a lower incidence of peritonitis in those treated with prophylactic antibiotics when compared to no treatment [50–52]. In the largest level I trial the incidence of peritonitis in the vancomycin vs cefazolin vs placebo groups were 1% vs 7% vs 12%, p value = 0.02 [52]. Gadallah et al. suggested a further advantage to the use of vancomycin since its prolonged half-life in dialysis patients allows it to be given in one dose 12 h pre-insertion and remains effective for up to 7 days post-insertion. This compares to cephalosporins where patients require multiple dosing to ensure adequate antimicrobial coverage for the first 4–5 days post-catheter insertion [52]. Nevertheless, one has to be cognizant of the emergence of vancomycin-resistant organisms and that this is the only study suggesting that vancomycin is superior to cephalosporins.

Recommendation All children should receive preoperative and, when appropriate, postoperative antibiotics with the insertion of a PD catheter. The first choice should be multiple doses of intravenous cephalosporins (first dose 3 h pre-insertion) with the second choice being one dose of vancomycin given at least 12 h prior to the catheter insertion in patients with little or no residual renal function (best available evidence: pediatric IV, adult I).

Guideline X: initiation of PD

There are no pediatric data available on how to best initiate PD and the literature in adults is limited. Concern for the aggressive and early use of catheters derives mainly from the perceived risk of both dialysate leaks and the subsequent risk of peritonitis. Tzamaloukis et al. reported a retrospective review of dialysate leaks in 386 PD adult patients over an 11-year period. They noted that a wait period of 10–14 days between catheter insertion and PD initiation, as well as low starting dialysate volumes, resulted in a reduced incidence of leaks within the first 30 days postoperatively [53]. Subsequently, this practice has been advocated by several authors, including an official update, by Gokal et al. for the International Society of Peritoneal Dialysis [16, 54]. It should be noted that neither review provides any references or evidence to confirm or refute these recommendations. In most instances, when initiating an elective start for a peritoneal dialysis patient, it would be reasonable to wait 10–14 days before commencing dialysis in order to allow for maximal wound healing, noting that the optimal duration of this waiting time is currently unknown.

Recommendation Timing for the initiation of dialysis post-catheter insertion should be left to the discretion of the center recognizing the need for wound healing. If initiation of dialysis is required within 7 days post-catheter insertion, low volumes should be commenced (500 ml/BSA) (opinion).

Guideline XI: intraperitoneal volume

The fill volume for pediatric PD has traditionally been recommended based on body weight (30–50 ml/kg body weight) [55, 56]. However, it has been shown that the use of body weight for determination of dialysate volume will underestimate the optimal dialysate volume for younger children [57] (level V). Kohaut et al. demonstrated in a prospective study that equilibration curves based on body surface area was independent of age and optimal at dwell volumes of 1,200 cc/m^2. In children over the age of 2 years, Fischbach et al. found that the maximum tolerable dialysate volume was closer to 1,400 ml/m^2 [58, 59]. Although the intraperitoneal volumes are variable for each patient, the evidence strongly suggests the use of body surface area for intraperitoneal volume calculations.

Recommendation Optimal dialysate volume for children over the age of 2 years should be targeted between 1,200 and 1,400 cc/m^2 (best available evidence: pediatric V).

Guideline XII: PD adequacy

Dialysis adequacy has been validated in numerous adult studies and is defined as the minimum dialysis dose below which there is significant morbidity and mortality [60, 61] (level I). This subsequently led to the development of practice guidelines by both the National Kidney Foundation and the Canadian Society of Nephrology advocating for a minimum Kt/V (dialysis and residual renal function) of 2.1 for automated PD and 2.0 for all forms of PD, respectively [3, 4]. In pediatrics, there are no randomized clinical trials validating adequacy with outcome. Van der Voort et al. retrospectively reviewed their pediatric PD patients and found that only 45% of patients achieved the recommended NKF-DOQI Kt/V targets [62] (level V). Unfortunately, as clinical outcomes were not provided, it is difficult to come to any conclusion with respect to the importance of achieving the suggested Kt/V targets in children. In contrast, other pediatric adequacy studies had no difficulties in achieving NKF-DOQI Kt/V targets [63–67] (level V). In fact, the patients in these studies often achieved much higher Kt/V and CrCl targets and demonstrated positive effects between these high levels and important pediatric outcome parameters such as growth, reversal of renal osteodystrophy changes, and cardiac function [63–67]. To complicate matters further, there is also concern amongst pediatric nephrology dialysis experts about the achievability of the adult guidelines in children who are anephric. Hence, although the pediatric literature on adequacy is not strong, there does not appear to be detrimental effects from utilizing the DOQI and CSN guidelines as the minimal value for children on PD.

Recommendation New updated DOQI guidelines for pediatric dialysis adequacy in peritoneal dialysis are soon to be published and we would like to refer to this new guideline for the updated specific Kt/V and weekly clearance targets.

Guideline XIII: PD prescription

It has been well recognized that there are major physiologic and psychosocial differences between pediatric and adult patients on PD. These include membrane characteristics, membrane relationship with body surface area [68–72] (level V) as well as nonmedical influences on the choice of dialysis modalities, in part related to the recognition that children attending school have different needs than adults in the workplace. All of these variables have resulted in the use of automated PD as the most common modality of PD utilized among pediatric patients in North America [1]. Lack of data comparing the different modalities of PD does not allow for any firm recommendation about the type of PD other than that based on opinion.

The other important aspect of PD prescription is that of determining membrane characteristics. This has important implications as to the dialysis regimen of any given patient. Twardowski et al. first developed the peritoneal equilibration test (PET) to characterize peritoneal transport rates [73]. There have been numerous reports to date on the use of PET in children [65, 71, 74–80]. Warady et al. addressed the lack of a standardized process and published pediatric reference data in 1996 from 95 children who underwent a standardized pediatric PET protocol [81]. The results of this study showed that membrane transport in children is very similar to that of adults although there may be age-related differences in mass transfer area coefficients.

Recommendation Membrane characteristics should be determined by the PET with a test exchange volume scaled to BSA (1,100 ml/m^2, 2.5% dialysate) and this should then determine a dialysis regimen with optimization of dwell time and exchange volumes (best available evidence: pediatric V).

Guideline XIV: total solute clearance and regimen

The reproducibility of adequacy measurements should be obtained at a time that serum samples reflect the overall average for the 24-h period. The ideal time for this is at the midpoint of the day (opinion). The Ad Hoc European Committee does not comment on the frequency of adequacy measurements [7]. The DOQI recommendations do not differentiate between adults and children in regards to the frequency of routine measurements [5]. Their recommendations are to perform an initial Kt/V 1 month after initiation of dialysis and then a minimum of two other times in the first 6 months. After 6 months, the recommendation is to measure total solute clearance every 4 months. This would appear to be reasonable in an adult population where their general state of health is static. In children, there are never-ending effects of growth (with subsequent revision of peritoneal dialysate volumes) with multiple changes in nutrition as well as effects on cognition and brain development that would support a more frequent monitoring of adequacy. Due to lack of available evidence, the recommendations here are based purely on previous experience and consensus.

Recommendation Delivered PD dose and residual renal function (the average of the weekly clearances of creatinine and urea derived from a 24-h urine collection with measurements of creatinine and urea in blood and urine, and urine volume) should be measured 1 month after reaching maximum volume on peritoneal dialysis and a minimum of two times over the subsequent 6 months. After 6 months, total solute clearance should be measured every 3 months and/or if there has been significant changes in the dialysis prescription and/or in the setting of a recent bout of peritonitis (must wait minimum 4 weeks from peritonitis). In the younger child on PD, the frequency of these measurements is the recommended minimum and is left to the discretion of the nephrologist if frequency is to be increased (opinion).

Conclusion

The goal of the Canadian Association of Pediatric Nephrologists with this review and recommendations was to comprehensively review and assess specific aspects of the PD prescription in children. These national guidelines will help promote optimal care for Canadian children on dialysis.

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