2. Peritoneal dialysis-associated peritonitis in children

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Guidelines

No recommendations possible based on Level I or II evidence

Suggestions for clinical care
(Suggestions are based on Level III and IV evidence)

- No recommendation.

Consensus opinion regarding the management of peritonitis in childhood is offered in the ISPD guidelines (Warady et al 2000) and is currently the most specific, clinically useful guide to the appropriate treatment of this patient group.

Background

The preferred treatment for childhood end-stage renal failure (ESRF) is successful transplantation, however, peritoneal dialysis (PD) is frequently undertaken when transplantation is not immediately available. Few paediatric patients remain on long-term PD.

Many of the difficulties and challenges seen in the PD of children are similar to those experienced in the adult population. Thus, many questions could be adequately answered by carefully constructed randomised controlled trials (RCTs) involving adult and paediatric PD patients.

However, some issues are specific to paediatrics – for example, the siting of the exit site is much more problematic in infants who have small thin anterior abdominal walls and the exit site is more prone to contamination from urine, faeces, gastrostomy feeds and vomit. In addition, older children tend to play with their catheters more than is usually seen in the adult population.

Search strategy

Databases searched: PubMed Medline from 1990-2002. Search terms were: peritoneal dialysis and (CAPD or CCPD or APD), peritonitis, antibiotic*, cefazolin, cephalothin, ceftazidime, vancomycin.

Date of search/es: 22 November 2002, 6 December 2002.

What is the evidence?

There are few studies that can be included in clinical practice guidelines for the treatment of peritonitis in a paediatric PD population as most of the available data is from observational or cohort studies (not Level I or II evidence). Schaefer et al (1999) and Klaus et al (1995) reported an RCT that investigated the use of glycopeptide/ceftazidime treatment in children with PD-associated peritonitis. They compared treatment of CAPD and APD patients with peritonitis as defined by the presence of cloudy dialysate with or without fever and abdominal pain, and presence of ≥ 100 cells/µL dialysate with ≥ 50% neutrophils. Glycopeptides (vancomycin or teicoplanin) were given in continuous or intermittent dosing and ceftazidime (250 mg/L) was given in every bag. They noted that in Gram-positive peritonitis (79% of cases) the overall primary success rate was 95% and the relapse rate was 21%. Residual renal function deteriorated regardless of treatment modality. There was no statistical difference between continuous or intermittent vancomycin or teicoplanin Schaefer et al (1999).

Summary of the evidence

Please refer to the Evidence Tables shown in the Appendices.

What do the other guidelines say?

Kidney Disease Outcomes Quality Initiative: No recommendation.

British Renal Association: These guidelines state: “There is no firm agreement on the best catheter configuration to use in children, as there are no conclusive data on the impact on peritonitis rates. Data from the North American Registry suggest that children should have PD catheters that have swan neck tunnels, two cuffs and downward pointing exit sites (Alexander et al 1998). The recommended time for removal of the PD catheter following successful transplantation is 3-6 weeks.”

Canadian Society of Nephrology: No recommendation.

European Best Practice Guidelines: No recommendation.

International Guidelines: ISPD guidelines (Warady et al 2000). Please refer to Tables 1-2 and Figures 1-3 in the Appendices.

Guideline 1: Diagnosis of Peritonitis
An empiric diagnosis of peritonitis should be made if the peritoneal effluent is cloudy, the effluent white blood cell (WBC) count is greater than 100/mm^3, and at least 50% of the WBCs are polymorphonuclear leukocytes. The diagnostic workup should be performed using a standardized procedure.

Guideline 2: Empiric Therapy of Peritonitis
In patients with cloudy effluent, without fever and/or severe abdominal pain, and no risk factors for severe infection (listed below), the combined intraperitoneal administration of a first-generation cephalosporin and ceftazidime is recommended (Figure 1). In patients with fever and/or severe abdominal pain, a history of methicillin-resistant *Staphylococcus aureus* (MRSA) infection, a recent history or current evidence of an exit-site/tunnel infection or nasal/exit-site colonization with *S. aureus*, and in patients younger than 2 years, a glycopeptide (vancomycin or teicoplanin) combined with ceftazidime should be administrated intraperitoneally (Figure 1). Aminoglycosides should not be used as initial treatment in children.

Guideline 3: Modification of APD Regimen for Treatment of Peritonitis
In patients who receive nocturnal automated peritoneal dialysis (APD) with short dwell times for routine therapy, the initial (24 - 48 hours) treatment of peritonitis should include a prolongation of the dialysate dwell time to 3 - 6 hours, until there is clearing of the peritoneal effluent. This does not apply to asymptomatic patients in whom the routine prescription can be continued, or to patients with ultrafiltration needs requiring more frequent exchanges. Patients receiving continuous ambulatory peritoneal dialysis (CAPD) do not require any change in their exchange frequency.

Guideline 4: Modification of Therapy for Gram-Positive Peritonitis
If a gram-positive organism is cultured, the empiric use of ceftazidime should be discontinued. A first-generation cephalosporin should be continued for non methicillin-resistant staphylococci; vancomycin, clindamycin, or teicoplanin for methicillin-resistant staphylococci; and ampicillin for enterococci and streptococci (Figure 2). Treatment duration should be 2 weeks for all organisms except *S. aureus*, which should be treated for 3 weeks.

Guideline 5: Modification of Therapy for Gram-Negative Peritonitis
If a single ceftazidime-sensitive gram-negative organism (e.g., Escherichia coli, Klebsiella, or Proteus species) is cultured, the empiric use of ceftazidime should be continued and the first-generation cephalosporin or glycopeptide should be discontinued. If the single organism is a pseudomonad (e.g. Pseudomonas aeruginosa), ceftazidime should be continued and a second antibiotic with activity against the isolated organism should be added. If anaerobic bacteria or multiple gram-negative organisms are isolated, intra-abdominal pathology should be considered and treatment should include the use of metronidazole (Figure 3). Treatment duration should be 2 weeks for a single gram-negative organism other than Pseudomonas/Stenotrophomonas species. Treatment duration should be 3 weeks for Pseudomonas/Stenotrophomonas species, multiple organisms, and/or anaerobes.

Guideline 6: Modification of Therapy for Culture-Negative Peritonitis
If the initial cultures remain sterile at 72 hours and signs and symptoms of peritonitis are improved, the combined empiric antibiotic therapy prescribed to cover the gram-positive and gram-negative spectra should be continued for 2 weeks.

Guideline 7: Modification of Therapy for Fungal Peritonitis
If fungi are identified by Gram stain or culture, treatment should be initiated with either intravenous amphotericin B or a combination of an imidazole/triazole (e.g. intraperitoneal or oral fluconazole) and flucytosine. In each case, it is recommended that treatment should be associated with early catheter removal. In patients in whom the catheter is not removed initially, immediate catheter removal should take place if improvement does not occur within 3 days of treatment initiation. Treatment duration following catheter removal for all patients

should be 2 weeks or longer following complete resolution of the clinical symptoms of infection. Treatment duration without catheter removal should be 4-6 weeks.

Guideline 8: Evaluation of Primary Treatment Response
The response to the initial antibiotic treatment should be evaluated daily after treatment initiation. Treatment can be considered successful if an improvement in clinical status (e.g. cessation of abdominal pain and fever, reduction of effluent cloudiness) has been achieved by 72 hours of therapy. A reduction of the dialysate WBC count by more than 50% is additional evidence of successful therapy.

Guideline 9: Approach to Patients Who Fail to Demonstrate Clinical Improvement
If no clinical improvement occurs within 72 hours of treatment initiation, potential sources of persistent infection should be evaluated. Treatment modifications may include an alteration of antibiotic therapy and/or catheter removal.

Guideline 10: Approach to the Patient with Relapsing Peritonitis
Relapsing peritonitis is defined as a recurrence of peritonitis with the same organism as in the immediately preceding episode, according to antibiotic susceptibilities, within 4 weeks of completion of antibiotic treatment. Since the causative organism is not known at the time of onset of symptoms, empiric treatment should be reinitiated according to Guideline 2. After bacteriologic confirmation of a relapse, treatment should be organism specific (see treatment recommendations below) and (except for Pseudomonas/Stenotrophomonas species) treatment duration should be 3 weeks (Table 3).

Guideline 11: Adjunctive Therapy for Peritonitis
In patients who are being treated for peritonitis, adjunctive therapy should be considered on an individual basis and may include the following:

a. Decreased peritoneal fill volume in patients with significant abdominal discomfort;
b. Oral antifungal prophylaxis during the course of antibiotics;
c. Low-dose intraperitoneal heparin as long as peritoneal effluent is cloudy; and
d. Intravenous immune globulin (IVIG) in patients with hypogammaglobulinemia.

Guideline 12: Indications for Catheter Removal and Replacement
Peritoneal dialysis catheter removal should occur as part of the recommended treatment course in situations in which failure to do so is unlikely to result in successful peritonitis therapy. The timing of catheter replacement should be 2-3 weeks following catheter removal in most cases.

Guideline 13: Prophylactic Antibiotic Therapy
Prophylactic antibiotic therapy for *S. aureus* nasal carriage is recommended to decrease the risk of *S. aureus* catheter exit-site/tunnel infections. Prophylactic antibiotic therapy should be given at the time of catheter placement in the form of a single dose of a first-generation cephalosporin. Antibiotic prophylaxis should also be considered following accidental intraluminal contamination, prior to dental procedures, and prior to procedures involving the gastrointestinal or urinary tract. Prophylactic systemic long-term antibiotic treatment is not indicated.

Guideline 14: Diagnosis of Catheter Exit-Site Infection
The diagnosis of a catheter exit-site infection should be made in the presence of a purulent discharge from the sinus tract, or marked pericatheter swelling, redness, and/or tenderness, with or without a pathogenic organism cultured from the exit site. Infectious symptoms should be rated according to an objective scoring system (Table 6).

Guideline 15: Treatment of Catheter Exit-Site Infection
Antibiotic treatment of a catheter exit-site infection should be started after culture results have been obtained, unless signs of severe infection are present. The antibiotic should be chosen according to the susceptibilities of the cultured organism. Treatment duration should be 2-4 weeks.

Implementation and audit

No recommendation.

Suggestions for future research

No recommendation.

References

Alexander SR, Donaldson LA, Sullivan KE. 1998. CAPD/CCPD for children in North America: the NAPRTCS experience. In: Fine RN, Alexander SR, Warady BA (eds). CAPD/CCPD in children. 2nd edition. Boston: Kluwer Academic Publishers, 5-8.

Klaus G, Schaefer F, Muller-Wiefel D et al. 1995. Treatment of peritoneal dialysis associated peritonitis with continuous versus intermittent vancomycin/teicoplanin and ceftazidime in children: preliminary results of a prospective randomized trial. Adv Perit Dial 11: 296-301.

Schaefer F, Klaus G, Muller-Wiefel DE et al. 1999. Intermittent versus continuous intraperitoneal glycopeptide/ceftazidime treatment in children with peritoneal dialysis-associated peritonitis. The Mid-European Pediatric Peritoneal Dialysis Study Group (MEPPS). J Am Soc Nephrol 10: 136-45.

Warady BA, Schaefer F, Holloway M et al. 2000. Consensus guidelines for the treatment of peritonitis in pediatric patients receiving peritoneal dialysis. Perit Dial Int 20: 610-24.

Appendices

Appendix 1

Table 1: ISPD recommended antibiotic doses (paediatric)

Antibiotic Dosing Recommendations Administration should be via intraperitoneal route unless specified otherwise			
	Continuous therapy		Intermittent therapy[b]
	Loading dose[a]	Maintenance dose	
Glycopeptides[b]			
Vancomycin	500 mg/L	30 mg/L	30 mg/kg q 5-7 days
Teicoplanin[c]	200 mg/L	20 mg/L	15 mg/kg q 5-7 days
Cephalosporins			
Cefazolin/ Cephalothin	250 mg/L	125 mg/L	15 mg/kg q 24 hrs
Cefuroxime	200 mg/L	125 mg/L	15 mg/kg q 24 hrs
Cefotaxime	500 mg/L	250 mg/L	30 mg/kg q 24 hrs
Ceftazidine	250 mg/L	125 mg/L	15 mg/kg q 24 hrs
Ceftizoxime	250 mg/L	125 mg/L	–
Antifungals			
Amphotericin B	1 mg/kg IV	1 mg/kg/day IV	–
Fluconazole	–	–	3-6 mg/kg IP, IV, or PO q 24-48 hrs (max dose 200 mg)
Flucytosine	50 mg/kg IV or PO (max dose 2.0 g)	25-37.5 mg/kg PO q 24 hrs (max dose 1.0 g)	–
Aminoglycosides[d]			
Amikacin	25 mg/L	12 mg/L	–
Gentamicin	8 mg/L	4 mg/L	–
Netilmycin	8 mg/L	4 mg/L	–
Tobramycin	8 mg/L	4 mg/L	–
Penicillins[d]			
Azlocillin	500 mg/L	250 mg/L	–
Piperacillin	–	250 mg/L	150 mg/kg IV q 12 hrs
Ampicillin	–	125 mg/L	–
Oxacillin	–	125 mg/L	–
Nefcillin	–	125 mg/L	–
Amoxicillin	250-500 mg/L	50 mg/L	–
Quinolones			
Ciprofloxacin	50 mg/L	25 mg/L	–
Combinations			
Ampicillin/Sulbactam	1000 mg/L	100 mg/L	–
Imipenem/Cilastatin	500 mg/L	200 mg/L	–
Trimethoprim/ Sulfamethoxazole	320/1600 mg/L	80/400 mg/L	–
Others			
Clindamycin	300 mg/L	150 mg/L	–
Metronidazole	–	–	15 mg/kg/day PO, IV, rectally in 3 doses (max 1.5 gram/day)
Rifampin	–	–	20 mg/kg/day PO (max dose 600 mg/day)
Aztreonam	1000 mg/L	250 mg/L	–

q = every; IV = intravenously; IP = intraperitoneally; PO = orally.

[a] Loading dose should be administered during a standardized 3- to 6-hour dwell period. Concentration-related loading doses assume usual patient-specific fill volume (i.e. approximately 1100 mL/m2 body surface area). If a smaller volume is instilled, the concentration must be increased to ensure infusion of an equal mass of antibiotic. Intermittent antibiotic dosing should be administered over ≥ 6 hours in one bag per day for CAPD patients, or during a full fill volume daytime dwell for APD patients, unless otherwise specified.
[b] Accelerated glycopeptide elimination may occur in patients with residual renal function. If intermittent therapy is used in this setting, the second dose of antibiotic should be time-based on a blood level obtained 3-5 days after the initial dose. Redosing should occur when the blood level is < 12 mg/L for vancomycin, or 8 mg/L for teicoplanin. Intermittent therapy is not recommended for patients with residual renal function unless serum drug levels can be monitored in a timely manner.
[c] Teicoplanin is not currently available in the United States.
[d] Aminoglycosides and penicillins should not be mixed in dialysis fluid because of the potential for inactivation.

The therapeutic recommendations provided above are those of the ISPD Advisory Committee on Peritonitis Management in Pediatric Patients and are, in large part, based upon adult experiences.

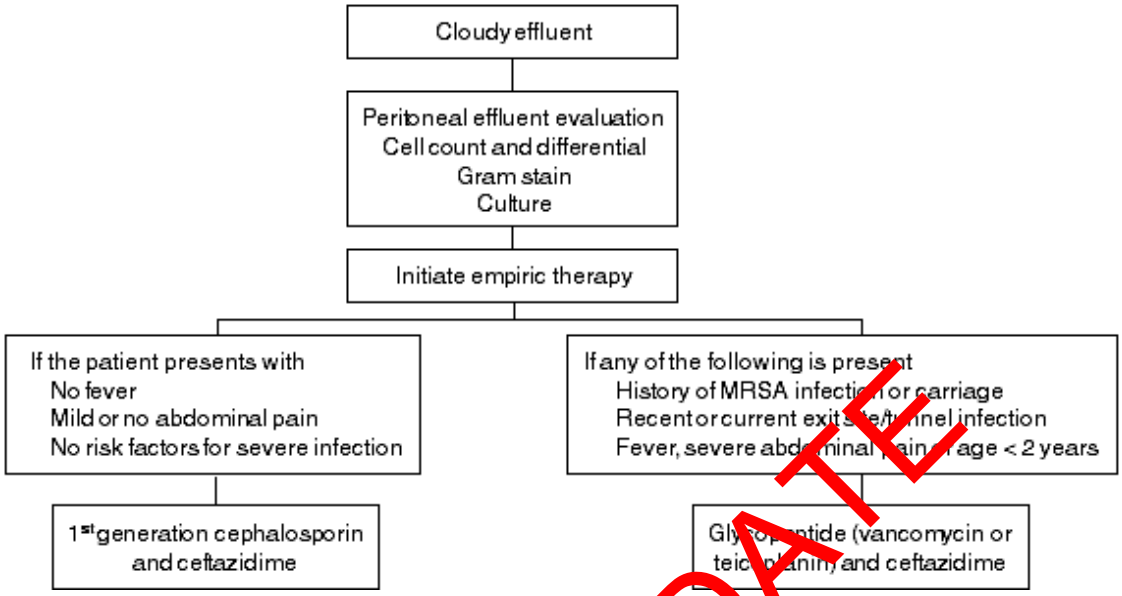
(Warady et al 2000)

Table 2: ISPD recommended duration of antibiotic therapy and timing of catheter replacement (paediatric)

Situations in Which Catheter Removal and Subsequent Replacement Should be Strongly Considered in Pediatric Peritoneal Dialysis Patients		
Clinical setting	Antibiotics	Interval between catheter removal and replacement (weeks)
Relapse of treated *Staphylococcus aureus* peritonitis with a *S. aureus* catheter-related infection	2 weeks (intravenous); simultaneous catheter removal and replacement with 3 weeks of antibiotics is possible in patient with low (<100/µL) effluent white blood cell count	2-3
Relapse of treated *Pseudomonas/Stenotrophomonas* peritonitis	2 weeks (intravenous)	2-3
Fungal peritonitis	≥ 2 weeks (intravenous/oral)	≥ 2-3
Refractory (at 72-96 hours) peritonitis (any pathogen or culture negative)	2 weeks (intravenous)	2-3
Refractory (at 72-96 hours) anaerobic peritonitis	2 weeks (intravenous)	2-3
Refractory (1 month) catheter exit site/tunnel infection	2 weeks (intravenous); simultaneous catheter removal and replacement is possible unless infection is severe with purulent discharge	2-3

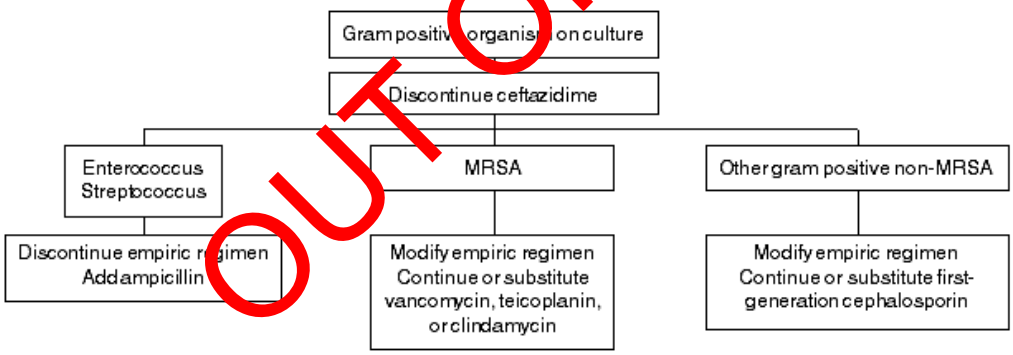
(Warady et al 2000)

Figure 1 Empiric therapy. MRSA = methicillin-resistant *Staphyloccous aureus*



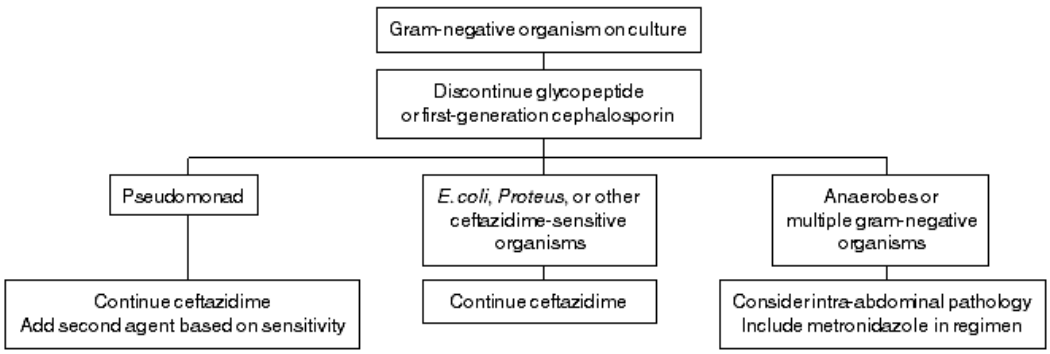
(Warady et al 2000)

Figure 2 Gram-positive organism on culture



(Warady et al 2000)

Figure 3 Gram-negative organism on culture



(Warady et al 2000)

Appendix 2

Table 3 Characteristics of randomised controlled trial evidence

Study ID (author, year)	N	Study Design	Setting	Participants	Intervention (experimental group)	Intervention (control group)	Follow up (months)	Comments
Schaefer et al 1999	152	Randomised controlled clinical trial	Multicentre	CAPD and APD patients with peritonitis	Continuous treatment with vancomycin/ ceftazidime or teicoplanin/ ceftazidime (i.p. load 15 mg/kg body weight for vancomycin, 7.5 mg/kg for teicoplanin, 250 mg/L dialysate for ceftazidime)	Intermittent treatment with vancomycin 30 mg/kg or teicoplanin 15 mg/kg and ceftazidime 500 mg/L	19	

Table 4 Quality of randomised trials

Study ID (author, year)	Method of allocation concealment	Blinding			Intention-to-treat analysis	Loss to follow up (%)
		(participants)	(investigators)	(outcome assessors)		
Schaefer et al 1999	Unclear	No	No	No	No	Unclear

Table 5 Results for dichotomous outcomes

Study ID (author, year)	Outcomes	Intervention group (number of patients with events/number of patients exposed)	Control group (number of patients with events/number of patients not exposed)	Relative risk (RR) [95% CI]	Risk difference (RD) [95% CI]
Schaefer et al 1999	Treatment failure	NA*	NA	NA	NA

* NA = Raw data not available for calculation of these estimates. The authors report that the risk of treatment failure according to the treatment did not differ between the continuously treated patients (RR 1.17, 95% CI 0.51 to 2.67) and the intermittently treated patients (RR 0.83, 95% CI 0.30 to 2.27).

Table 6 International Society for Peritoneal Dialysis exit-site scoring system*

	0 points	1 point	2 points
Swelling	No	Exit only (<0.5 cm)	Including part of or entire tunnel
Crust	No	<0.5 cm	>0.5 cm
Redness	No	<0.5 cm	>0.5 cm
Pain on pressure	No	Slight	Severe
Secretion	No	Serous	Purulent

* Infection should be assumed with a cululative exit site score of 4 or greater