Prophylactic antibiotics for insertion of peritoneal dialysis catheter

Date written: October 2010
Final submission: September 2012
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GUIDELINES

a. Intravenous antibiotic prophylaxis should be used prior to peritoneal dialysis catheter insertion to reduce the risk of early peritonitis. (Level I evidence)
b. Vancomycin, cephalosporin and gentamicin have demonstrated effectiveness in reducing the risk of peritonitis. (Level II evidence)

SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on level III and IV evidence)

- **Protocols for antibiotic prophylaxis prior to catheter insertion should be guided by the local infectious disease guidelines. Use of vancomycin should be restricted to avoid emerging vancomycin-resistant enterococci (VRE) and *Staphylococcus aureus* (VRSA). Vancomycin use should be guided by the individual unit's infectious disease guidelines.**

IMPLEMENTATION AND AUDIT

Individual renal units should have a protocol for antibiotic prophylaxis prior to peritoneal dialysis (PD) catheter insertion which provides suitable cover for the bacteria isolated in that unit. All PD units should document antibiotic prophylaxis and the type of antibiotic administered in addition to data on all PD-related problems including exit site infections, tunnel infections, peritonitis, catheter malfunction rates and catheter survival times. These data should be submitted to the ANZDATA registry.

BACKGROUND

Many people with end-stage kidney disease use PD as their mode of renal replacement therapy. Despite advances in connectology, peritonitis remains the Achilles heel of PD with rates greater than 0.6 episode/patient-year reported in Australia and New Zealand [1]. Different antimicrobial interventions are used to reduce the risk of peritonitis. Antibiotic prophylaxis carries a toxicity risk as well as the risk of emerging bacterial resistance. Antibiotics may also be ineffective in some cases. The aim of this guideline was to assess the use of prophylactic antibiotics for the insertion of a PD catheter and their effectiveness in reducing the incidence of early infectious complications such as peritonitis.

SEARCH STRATEGY

Databases searched: MeSH terms and text words for peritoneal dialysis were combined with MeSH terms and text words for peritonitis, catheter and anti-infective agent. These were then combined with the filters for randomised controlled trials, meta analyses and cohort studies. The

search was carried out in Medline (1950 - September Week 4, 2010) and restricted to the years 2003-2010. The Cochrane Renal Group specialised register of renal-related randomised controlled trials was also searched for trials not included in Medline.

Date of searches: October 2010; update search August 2012.

WHAT IS THE EVIDENCE?

Systematic reviews

A 2004 Cochrane review of antimicrobial agents used to prevent peritonitis in PD included nineteen randomised controlled trials (RCTs) which reported on 1949 participants [2].

Oral antibiotics

The 2004 Cochrane review identified different trials involving 315 participants who were randomly assigned to receive oral prophylactic antibiotics (co-trimoxazole, cephalexin, ofloxacin or rifampicin) compared with placebo or no treatment. Oral antibiotics did not reduce the risk of peritonitis, as shown in four of the trials involving 235 patients (RR 0.76, 95% CI: 0.38 - 1.53). In two trials, oral antibiotics did not reduce the risk of peritonitis (670 patient-months; RR 0.74, 95% CI: 0.39 - 1.37) but significantly reduced the risk of exit site and tunnel infection (2 trials; 31 patients; RR 0.29, 95% CI: 0.09 - 0.97) [2].

Intravenous antibiotics

The same Cochrane review identified four RCTs that examined perioperative intravenous antibiotic prophylaxis compared with no treatment [2]. They showed that intravenous antibiotic prophylaxis significantly reduced the risk of early peritonitis (<I month post-operatively) compared with no treatment in 335 patients (RR 0.35, 95% CI: 0.15 - 0.80) but not the risk of exit site infection (2 trials; 114 patients; RR 0.32, 95% CI: 0.02 - 4.81).

The findings of the 2004 Cochrane review were further explored by the same authors [3]. Since these reviews were published, there have been no further studies published in this field.

Topical antimicrobial agents

Please refer to the ‘Prophylaxis for exit site/tunnel infections using mupirocin’ part of this guideline.

Randomised controlled prospective studies

Gadallah et al randomised 221 participants to receive either prophylactic intravenous vancomycin 1 g 12 hours before catheter placement or cephazolin 1 g 3 hours before the procedure or no antibiotics [4]. There was significantly less peritonitis at 14 days in the vancomycin group and the cephazolin group compared with the group not given antibiotics (1% vs 7% vs 12%, P = 0.02). Single dose vancomycin was superior to single dose cephalosporin, however, peritonitis was only documented for the first 14 days.

In an earlier study, Wikdahl et al administered cefuroxime 1.5 g intravenously preoperatively and 250 mg intraperitoneally in the first 1 litre dialysis bag or no antibiotic [5]. Of those who received antibiotics, no patient had peritonitis within 10 days. In the control group, four patients developed peritonitis. A study published in 1988 showed that gentamicin administered at the time of catheter insertion (1.5 mg/kg) reduced peritonitis from 46% to 8% (P <0.05) in the first four post-operative weeks, compared with no antibiotic prophylaxis [6]. Similarly, there was a significant reduction in exit site infection (ESI) from 53% to 0% (P <0.01). Lye et al (1992) randomised 50 patients and showed no benefit from antibiotic prophylaxis with single-dose cephazolin and gentamicin

compared with no antibiotics [7]. No recent trials addressing this issue were identified in the literature searches for this topic.

Retrospective studies

Two registry-based studies and one retrospective study were mentioned in the previous CARI guideline published in 2004 [8]. A retrospective report on bedside Tenckhoff catheter implantation without antibiotic prophylaxis in Thailand showed the development of an infection in 9/114 patients, three cases of ESIs with peritonitis and one patient had their catheter removed [9].

SUMMARY OF THE EVIDENCE

There is a systematic review of 4 RCTs addressing the issue of whether prophylactic IV antibiotics before the insertion of PD catheters reduce peritonitis. The same data are presented in a Cochrane review. These show that there is a significant reduction in the incidence of early peritonitis in three of the four trials. The largest of the RCTs shows an advantage of prophylactic vancomycin compared with cephazolin. Caution with vancomycin use is still encouraged to avoid emerging vancomycin-resistant enterococci (VRE) and vancomycin-resistant *S. aureus* (VRSA). There was no benefit shown with use of prophylactic oral antibiotics in relation to peritonitis. Oral antibiotics were shown to reduce exit site and tunnel infections in two trials.

WHAT DO THE OTHER GUIDELINES SAY?

Kidney Disease Outcomes Quality initiative: No recommendation.
UK Renal Association: Initial catheter insertion should be accompanied by antibiotic prophylaxis. (1B) [10]
Canadian Society of nephrology: No recommendation.
European Renal Best Practice Guidelines: EDTA-ERA. Antibiotic prophylaxis should be done preoperatively. (Evidence level A) [11]
International Guidelines: (ISPD 2010) Renal units should have clear protocols for perioperative catheter care, including the use of antibiotic prophylaxis (1A). Choice of antibiotic should be based on local guidelines, with consideration given to efficacy, risks of selection of resistant organisms, and development of *Clostridium difficile* colitis. [12]

SUGGESTIONS FOR FUTURE RESEARCH

1. Well-designed studies that address the efficacy, toxicity and cost of various antibiotic regimens.
2. A multicentre RCT assessing the efficacy of first generation cephalosporin in multi-resistant *S. aureus* (MRSA) and non-MRSA carriers.

CONFLICT OF INTEREST

Maha Yehia has no relevant financial affiliations that would cause a conflict of interest according to the conflict of interest statement set down by CARI.

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APPENDICES

Table 1 Characteristics of included studies

Study ID (author, year)	N	Study Design	Setting	Participants	Intervention (experimental group)	Intervention (control group)	Follow up (months)	Comments
Gadallah et al 2000	221	Randomised controlled trial	University medical centre, USA	Patients with newly placed PD catheters	Group I Single IV vancomycin 1000 mg 12 hrs before procedure	Group III (control). Not administered antiobiotics preoperatively <1 week before procedure	72	Group II Single IV cefazolin 1000 mg 3 hrs before procedure
Wikdahl et al 1995	38	Randomised controlled trial	University hospital, Sweden	Patients entering PD program	Cefuroxime 1.5 g IV preoperatively	No prophylactic antibiotics	10 days	
Bennett-Jones et al 1988	27	Randomised controlled trial	Regional hospital, UK	Patients receiving Tenckhoff catheter prior to PD. Included first and replacement catheters.	Gentamicin 1.5 mg/kg IV at time of anaesthesia	No prophylactic antibiotics	28 days	
Lye et al 1992	50	Randomised controlled trial	University hospital, Singapore	All ESKD patients who had Tenckhoff catheters inserted over a 13-month period.	Preoperative cefazolin (500 mg) and gentamicin (80 mg)	No prophylactic antibiotics	3 months	

Table 2 Quality of randomised trials

Study ID (author, year)	Method of allocation concealment *	Blinding			Intention-to-treat analysis †	Loss to follow up (%)	Comments ‡
		(participants)	(investigators)	(outcome assessors)			
Gadallah et al 2000	Not specified	No	No	No	Unclear	Not specified	(–)
Wikdahl et al 1995	Consecutive	No	No	No	No	0%	(–)
Bennett-Jones et al 1988	Consecutively numbered sealed envelopes.	No	Yes	Yes	No	4%	(Ø)
Lye et al 1992	Consecutive	No	No	No	No	0%	(–)

* Choose between: central; third party (e.g. pharmacy); sequentially labelled opaque sealed envelopes; alternation; not specified.
† Choose between: yes; no; unclear.
‡ Quality score – "How successfully do you think the study minimised bias?" Choose between: very well (+); okay (Ø); poorly (–).

Table 3 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]
Gadallah et al 2000	Peritonitis	1/86 (Group I)	10/83	0.10 (0.01, 0.74)	-0.11(-0.18, -0.04)
Gadallah et al 2000	Peritonitis	6/85 (Group II)	10/83	0.59 (0.22, 1.54)	-0.05 (-0.14, 0.04)
Bennett-Jones et al 1988	Peritonitis	1/13	6/13	0.17 (0.02, 1.20)	-0.38 (-0.69, -0.08)
Wikdahl et al 1997	Microbial growth in dialysis fluid	0/18	6/20	0.09 (0.01, 1.41)	-0.30 (-0.51, -0.09)
Bennett-Jones et al 1988	Exit site infection	0/13	7/13	0.07 (0.00, 1.06)	-0.54 (-0.82, -0.26)
Lye et al 1992	Early exit site infection	6/25	7/25	0.86 [0.34, 2.19]	-0.04 [-0.28, 0.20]
Lye et al 1992	Late exit site infection	2/25	1/25	2.00 [0.19, 20.67]	0.04 [-0.09, 0.17]
Lye et al 1992	Early peritonitis	2/25	1/25	2.00 [0.19, 20.67]	0.04 [-0.09, 0.17]
Lye et al 1992	Late peritonitis	3/25	1/25	3.00 [0.33, 26.92]	0.08 [-0.07, 0.23]