

# Peritoneal dialysis catheter–related infection: exit site and tunnel

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## GUIDELINE

No recommendations possible based on Level I or II evidence

## SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on Level III and IV evidence)

- Effective antibiotic therapy is recommended for cases of peritoneal dialysis catheter-related infection.
- Either intraperitoneal or oral antibiotics may be considered.

## IMPLEMENTATION AND AUDIT

Primarily, audit should consist of ongoing research to continually improve and validate our ability to predict outcomes based on medical parameters.

## BACKGROUND

Exit site infection (ESI) has been defined as clinically apparent infection at the exit site with or without a positive culture. Included in this definition is catheter tunnel tract infection. Clinical signs of infection include purulent drainage, redness, swelling, warmth and tenderness over or around the exit site. Exit site and tunnel infections are a significant cause of morbidity and are responsible for a significant proportion of patient dropout from peritoneal dialysis. [1] The bacteria that colonise the exit site are the same as those responsible for ESIs, but are different to those that cause peritonitis. [2]

There are various stages in the development of an infected exit site, which include serous and purulent drainage, abscess formation and tunnel infection. Early identification and diagnosis of the various infection stages are vital for the initiation of prompt and effective therapy. Ultrasonography of the exit site has been used to diagnose exit site and tunnel infections. A sonolucent zone around the external cuff over 1 mm thick following treatment with a course of antibiotic treatment and also with the involvement of the proximal cuff are associated with poor clinical outcome. [3] With the ultrasonographic studies, a tunnel infection is confirmed when the subcutaneous pathway is clinically occulted. [4]

Prevention of infection is considered essential for the successful maintenance of peritoneal dialysis (PD). Strategies to prevent or reduce the risk of infection include rigorous exit site care, catheter care and meticulous attention to the use of a clean no-touch technique for dialysis exchanges. Both antibiotic and antimicrobial agents and dressing technique play important roles in the survival of the PD catheter.

The objective of this guideline was to review current evidence in the prevention and management of catheter exit site infection and tunnel infection.

## **SEARCH STRATEGY**

**Databases searched:** MeSH terms and text words for peritoneal dialysis were combined with MeSH terms and text words for catheter, peritonitis, exit site infection and tunnel infection. The search was carried out in Medline (1950 – September Week 3, 2010). The Cochrane Renal Group Trials Register was also searched for trials not indexed in Medline.

**Date of searches:** 15 October 2010.

## **WHAT IS THE EVIDENCE?**

### **Evaluation of the exit site/tunnel and diagnosis of infection**

Twardowski et al performed 565 evaluations of healed exit sites in 56 patients. [5,6] A new classification was developed with six distinct categories of exit site appearance: acute infection, chronic infection, external cuff infection, traumatised exit, etc. The outcomes in each category were correlated with treatment measures in a 5-year longitudinal study. A cross-sectional study was conducted with 45 patients, using loupe and magnifier evaluations. Ninety-one percent (41/45) of the evaluations were in agreement.

Vychytil et al investigated indications and outcomes of 738 ultrasound examinations of the PD catheter tunnel. [7] The research team concluded that tunnel ultrasonography is useful to assess whether tunnel infection is present, and the severity of involvement. By using ultrasonography, a therapeutic regimen can be evaluated and reviewed.

### **Therapy for exit site/tunnel infection**

Flanigan et al reported a randomised, prospective study comparing intraperitoneal vancomycin plus oral rifampin or oral trimethoprim/ sulfamethoxazole for Gram-positive catheter infections. [8] There were 126 recorded catheter infections resulting in a rate of 0.67 episodes per patient year of exposure. The cure rate of Gram-positive catheter infections treated with vancomycin plus rifampin (86% cured) was indistinguishable from that achieved with oral trimethoprim/sulfamethoxazole (89% cured;  $P = 0.99$ ). Precautions need to be considered to retard the development of vancomycin-resistant enterococcus (VRE), if prolonged use of vancomycin is planned.

Plum et al in a prospective randomised study, showed the greater efficacy of the intraperitoneal (IP) application of clindamycin as a first-line antibiotic compared with the oral route for the treatment of tunnel infections. [9] The results showed no significant difference in the pericatheter fluid along the catheter at study entry, with 4 mm (median; range: 2-6 mm) in the oral group and 4 mm (range: 2-4 mm) in the IP group. The IP treatment resulted in a decrease to 0 mm (0-2 mm) after 28 days ( $P < 0.05$ ), while the diameter was still 2 mm (0-10 mm; ns) in the oral group. The disappearance of ESI also occurred earlier in the IP group (51 vs 15 days; ns). Catheter removal occurred once in the IP group and twice in the oral group within 6 months of study entry. There was no difference in clinical outcomes.

### **Disinfectant**

Luzar reported a multicentre RCT where adult continuous ambulatory peritoneal dialysis (CAPD) patients were randomised to disinfect the exit site 2–3 times per week with a 20 g/L solution of povidone iodine and then cover the exit site with sterile gauze, or cleanse the exit site daily with non-disinfectant soap on sterile gauze. [10] There was a reduction in the rate of ESIs with the use of povidone-iodine solution compared with the soap and water cleansing ( $P = 0.07$ ).

Wilson randomised 149 adult PD patients and examined the effectiveness of standard dressing changes versus standard dressing changes plus povidone-iodine dry powder spray (2.5%) in the prevention of ESIs and/or peritonitis. [11] Povidone-iodine did not reduce the number of total infections, ESIs or peritonitis compared with the control group over the period of the study.

### **Other considerations**

Dong et al reported a prospective observational study in Chinese CAPD patients. A total of 130 patients were examined during their PD bag exchange procedure 6 months after dialysis initiation. [12] Various items were observed such as dirty nails, improper hand washing, insufficient ultraviolet radiation, not wearing a face mask, checking for bag expiration or leakage, not flushing before filling and suspected connection contamination. It was concluded from a multivariate Cox regression analysis that not wearing a face mask or cap was significantly associated with a first episode of peritonitis [HR: 7.26, 95% CI: 2.6-20.1; P < 0.001].

Keane et al reported a summary of treatment recommendations for ESI from a consensus panel of experts. [13] The treatment recommendations for Gram-positive purulent drainage at the exit site are 2-4 weeks of a cephalosporin or vancomycin combined with oral rifampicin in the case of persistent infection, and ciprofloxacin for the treatment of Gram-negative infections.

Ibels et al conducted a survey in 1995 of 35 PD units in Australia. [1] In all units, a swab culture was obtained at the first sign of PD catheter ESI and exit site care procedures were reviewed with patients. Exit site infection rates were monitored, data collated, and procedures evaluated routinely in two-thirds of units. While the antibiotics used varied, most units used vancomycin or oral flucloxacillin. Catheter exit site and tunnel infections accounted for 12% and 6%, respectively, of the principal indications for removal of the peritoneal catheter. No correlations were undertaken between practices and outcomes.

Turner et al randomised 66 patients into one of three catheter groups: immobilizer, tape, or non-immobilized group. [14] The incidence of ESI over 347 patient-months was recorded. The results show no significant difference in infection rate between the three groups. While the findings of the study point to a need for a better quality immobilizer, the short duration of the study precluded any definitive conclusion being drawn.

Scalamogna et al reported data on surgical intervention, such as external cuff shaving in tunnel infections. [15,2,16] Shaving the cuff as a rescue treatment was effective for almost 50% of patients with antibiotic-resistant *Staphylococcus aureus* ESI. The catheters of the remaining patients were removed because of peritonitis associated with tunnel infection.

## **SUMMARY OF THE EVIDENCE**

There are no randomised controlled trials comparing the different classification and evaluation systems for ESI. The International Society for Peritoneal Dialysis (ISPD) has developed a simple scoring system for the signs and symptoms of PD exit site. The scoring system is easy to use and provides guidance on timing to treat immediately rather than waiting for a swab result. It also recommends that purulent discharge is an absolute indicator for antibiotic treatment. [4]

There are two randomised controlled trials that have compared antibiotic therapy treatment for exit site/tunnel infection. One study compared intraperitoneal vancomycin plus oral rifampin or oral trimethoprim/sulfamethoxazole for Gram-positive catheter infections. There was no difference with either treatment on catheter infection cure rate. The second study showed that there is greater efficacy with the intraperitoneal application of clindamycin as a first-line antibiotic compared with the oral route, for the treatment of tunnel infections.

Randomised controlled trials evaluating the effectiveness of povidone-iodine have provided inconclusive results. Povidone-iodine spray powder was not found to be better than standard dressing in relation to ESI, peritonitis or tunnel infection. Therefore, no definitive conclusions regarding the effectiveness of povidone iodine in reducing the rate of ESI or peritonitis in PD patients can be established on present evidence.

## **WHAT DO THE OTHER GUIDELINES SAY?**

**Kidney Disease Outcomes Quality Initiative:** No recommendation.

**UK Renal Association: 2010.** [17] Topical antibiotic administration should be used to reduce the frequency of *S. aureus* and Gram negative exit-site infection and peritonitis (1A). Exit site infection is suggested by pain, swelling, crusting, erythema and serous discharge; purulent discharge always indicates infection. Swabs should be taken for culture and initial empiric therapy should be with oral antibiotics that will cover *S. aureus* and *P. aeruginosa* (1 B).

**Canadian Society of Nephrology:** No recommendation.

**European Renal Best Practice Guidelines:** Exit site infection should be treated according to the guidelines of the International Society for Peritoneal Dialysis. [18]. Adjustments can be considered depending on the sensitivity patterns of microorganisms in the unit. (Evidence C)  
Topical treatment may be applied in equivocal cases or as adjuvant therapy. (Evidence C)

**International Guidelines: ISPD Guidelines/Recommendations (2005).** [4]

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. 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.

## **SUGGESTIONS FOR FUTURE RESEARCH**

1. Prospectively gather data to allow better prediction of outcomes after an ESI or tunnel infection. This should include more specific data than is currently collected, including symptoms, history of previous infection, and mode of contamination.
2. Perform a long term randomised controlled trial with sufficient power and blinding to look at the most effective antibiotic treatment for exit site and tunnel infection.
3. Run a diagnosis study such as using ultrasound examinations of the peritoneal catheter tunnel and a classification of ESI system.
4. Conduct studies and publish results on different ESI treatment protocols.

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**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
Flanigan MJ et al 1994	93	Randomised controlled clinical trial	Single centre America	PD patients	Vancomycin plus Rifampin	Trimethoprim / Sulfamethoxazole	45	
Plum J et al 1997	100	Randomised controlled clinical trial	Multi centre Germany	PD patients with catheter tunnel infections	Oral Clindamycin	Intraperitoneal Clindamycin	24	
Luzar MA et al 1990	127	Randomised controlled clinical trial	Multicentre, Europe	PD patients	Povidone iodine	Simple soap	16	
Wilson APR et al 1997	149	Randomised controlled clinical trial	UK	PD patients	Povidone iodine dry spray	Standard protocol (alcohol wipes)	12	

**Table 2 – 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)		
Flanigan MJ et al 1994	Alternation	Not stated	Not stated	Not stated	Unclear	0%
Plum J et al 1997	Open label trial	No	Not stated	Not stated	Unclear	9%
Luzar MA et al 1990	Central	Not stated	Not stated	Not stated	Unclear	0%
Wilson APR et al 1997	Central	No	Not stated	Not stated	Yes	2.7%

\* Choose between: central; third party (e.g. pharmacy); sequentially labelled opaque sealed envelopes; alternation; not specified.

† Choose between: yes; no; unclear.

**Table 3a – Results for dichotomous outcomes**

Study ID (author, year)	Outcomes	Intervention group (no. of patients with events/no. of patients exposed)	Control group (no. of patients with events/no. of patients exposed)	Relative risk (RR) [95% CI]	Risk difference (RD) [95% CI]
Flanigan MJ et al 1994	Peritonitis rate	22/44	24/53	1.10 (95% CI: 0.73, 1.68)	0.05 (95% CI: -0.15, 0.25)
Luzar MA et al 1990	Peritonitis rate (episode per patient year)	17/74 0.44	14/53 0.57	0.87 (95% CI: 0.47, 1.61)	-0.03 (95% CI: -0.19, 0.12)
Luzar MA et al 1990	Exit site infection Exit site infection rate (episode per patient year)	15/74 0.27	14/53 0.71	0.77 (95% CI: 0.41, 1.45)	-0.06 (95% CI: -0.21, 0.09)
Wilson APR et al 1997	Peritonitis rate (patient months per episode)	13/77 1:59.9	15/72 1:58.5	0.6 (95% CI: 0.31, 1.15)	-0.11 (95% CI: -0.26, 0.03)
Wilson APR et al 1997	Exit site infection (patient months per episode)	14/77 1:55.6	15/72 1:58.6	0.87 (95% CI: 0.45, 1.68)	-0.03 (95% CI: -0.15, 0.10)