12. Prophylaxis for exit site/tunnel infections using mupirocin

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Guidelines
(Include recommendations based on level I or II evidence)

Prophylactic therapy using mupirocin ointment, especially for *Staphylococcus aureus* carriage intranasally is recommended to decrease the risk of *S. aureus* catheter exit site/tunnel infections and peritonitis. (Level II evidence)

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

- The daily use of mupirocin does not appear to lead to significant levels of resistance in the short term (Vas et al 1999), but the levels of resistant organisms isolated become more significant with longer periods (Perez-Fontan et al 2002). After 4 years of continuous use, a significant problem can develop (Annigeri et al 2001).

- Prophylactic therapy using mupirocin ointment, especially for *S. aureus* carriage at the exit site is recommended to decrease the risk of *S. aureus* catheter exit site/tunnel infections and peritonitis (Bernardini et al 1996).

Background

Catheter exit site/tunnel infections are a major cause of *S. aureus* peritonitis in peritoneal dialysis (PD) patients. Hence, the prevention of exit site infection (ESI) and tunnel infection due to *S. aureus* is important. A number of studies have reported that the application of mupirocin ointment nasally or to the catheter exit site prophylactically, reduces *S. aureus* ESI and peritonitis when compared with historical controls. This guideline is limited to patients with proven nasal carriage.

Search strategy

Databases searched: MeSH terms and text words for PD catheters were combined with MeSH terms and text words for tunnel and exit site and then combined with MeSH terms and text words for peritonitis. The search was done in Medline (1966 – Week 1 November 2002). The Cochrane Renal Group Register of randomised controlled trials was also searched for trials not indexed in Medline.

Date of search/es: 3 December 2002.

What is the evidence?

Prophylactic intranasal mupirocin treatment:
The Mupirocin Study Group (1996) performed a randomised controlled trial (RCT) evaluating 267 PD patients who had been diagnosed as nasal carriers of *S. aureus* (determined by two positive nasal swabs on two separate occasions). Patients randomised to the intervention group were treated with nasal mupirocin ointment twice daily for 5 consecutive days every 4 weeks. Forty-four episodes of ESI due to *S. aureus* were reported in the control group compared with 14 in the mupirocin group (p = 0.006). There were no differences in the rates of tunnel infection or peritonitis. There was no evidence of a progressive increase in resistance to mupirocin with time. It was concluded that regular use of nasal mupirocin in PD patients who are nasal carriers of *S. aureus* significantly reduces the number of ESIs that occur because of this organism.

Perez-Fontan et al (1992) ran a randomised trial comparing intranasal mupirocin ointment with neomycin sulphate nasal ointment to treat *S. aureus* nasal carriers. Re-treatment with mupirocin was successful in 66% of cases compared with 20% of those given neomycin. There was a very low incidence of *S. aureus* peritonitis or catheter-related infections in the patients treated with mupirocin.

There is also a trial by Sesso et al (1994) which tested the efficacy of sodium fusidate nasal ointment given twice daily for 5 days against placebo and oral ofloxacin at a dose of 200 mg/day for 5 days. This trial showed no statistically significant difference between sodium fusidate nasal ointment and placebo in the risk of peritonitis, exit site/tunnel infection, catheter removal and all-cause mortality. *

* While this study did not use mupirocin, it is a significant randomised prospective trial investigating the prophylactic use of antibiotics for exit site/tunnel infection.

Prophylactic topical mupirocin treatment
Bernardini et al (1996) conducted a prospective randomised trial, controlling for *S. aureus* nasal carriage. Eighty-two PD patients were randomised to receive prophylaxis for *S. aureus* infections using either 600 mg cyclic oral rifampin for 5 days every 3 months or mupirocin ointment 2% applied daily to the exit site. ESI rates were 0.13/year with mupirocin and 0.15/year with rifampin (p = ns). The centre's historical rate was 0.46/year. Rates for peritonitis and catheter loss for both treatment groups were significantly lower than the centre's historical rate of 0.12/year (p < 0.001). Mupirocin ointment at the exit site and cyclic oral rifampin were

considered to be equally effective in reducing ESI, peritonitis and catheter loss due to *S. aureus*. However, mupirocin ointment at the exit site was inferior to the alternate therapy in this study, particularly in patients who cannot tolerate oral rifampin therapy (12%).

Summary of the evidence

Two RCTs were found that assessed the use of intranasal mupirocin treatment to prevent ESI, tunnel infection and peritonitis. One study evaluated the benefits of eliminating the nasal carriage of *S. aureus* with mupirocin ointment compared with placebo, while the other compared mupirocin with neomycin sulphate nasal ointment. There was a statistically significant reduction in the rate of ESIs due to *S. aureus* in the two studies.

One RCT compared topical mupirocin treatment against oral rifampin therapy to prevent ESI, tunnel infection and peritonitis. There was no difference between the groups in the rate of ESI, peritonitis and catheter loss due to *S. aureus*.

Non-randomised studies

Davey et al (1999) conducted a cost-effectiveness analysis of the Mupirocin Study Group trial. Overall costs of antibiotic treatment (for all infections combined) were not significantly different ($p = 0.2$) and total antibiotic costs (including mupirocin) were significantly higher in the mupirocin group ($p = 0.01$).

Casey et al (2000) reported on a prospective, historically-controlled study involving the daily application of mupirocin cream to the catheter exit site of 291 PD patients. Data was collected over an 11-month period and compared with data for all patients from the 11 months prior to the change. There was a 49% relative reduction in the rate of ESI ($p < 0.001$) and 31% reduction in episodes of peritonitis ($p = 0.003$) in the mupirocin treatment group. There was also a 68% reduction ($p = 0.05$) in the rate of *S. aureus* peritonitis and 37% ($p = 0.19$) decrease in catheter loss in the mupirocin group.

Thodis et al (1998) performed a prospective historically-controlled study of 181 PD patients to evaluate the effectiveness of applying mupirocin ointment to the exit site either daily or three-times-weekly for 1 year. Infection rates found during the study year were compared with the retrospective data. It was reported that the daily application of mupirocin cream significantly reduced the incidence of ESIs due to *S. aureus* by 91% and reduced peritonitis by 69%. In addition, the overall rate of peritonitis was significantly reduced ($p < 0.01$). There was no mupirocin resistance 1 year after the institution of local mupirocin use at the catheter exit site to prevent ESI.

What do the other guidelines say?

Kidney Disease Outcomes Quality Initiative: No recommendation.

British Renal Association: No recommendation.

Canadian Society of Nephrology: No recommendation.

European Dialysis and Transplant Association – European Renal Association: European Guidelines on Best Practice for the Management of Peritoneal Dialysis: 2002
Mupirocin ointment, either intranasal or at the exit site, reduces exit site infections especially in patients who are *S. aureus* carriers. (Level A)

International Society for Peritoneal Dialysis Guidelines/Recommendations: (Keane et al 2000)
Prophylactic antibiotic therapy for *S. aureus* nasal carriage is recommended to decrease the risk of *S. aureus* catheter exit site/tunnel infections.

Implementation and audit

1. Units could perform an audit of their *S. aureus* infection rate.

2. Mupirocin resistance emergence could be audited at a higher level.

Suggestions for future research

Perform a long-term study to further investigate the potential for the development of resistance to mupirocin including taking routine swabs to identify and document the presence of resistant organisms.

References

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Appendix

Table 1 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
Bernardini et al 1996	82	Randomised controlled clinical trial	University	CAPD patients proven to be S. aureus nasal carriers; 34% diabetic	Mupirocin (2%) calcium ointment applied daily to exit site	Rifampin (oral) 300 mg 2 times/day x 5 days, every 3 months	25	None
Mupirocin Study Group 1996	267	Randomised controlled clinical trial	Multicentre	CAPD patients proven to be S. aureus nasal carriers; 20% diabetic	Calcium mupirocin nasal ointment (2%) 2 times/day x 5 days, every 1 month	Placebo ointment	18	None
Perez Fontan et al 1992	22	Randomised controlled clinical trial	Teaching hospital	CAPD patients proven to be S. aureus nasal carriers; 26% diabetic	Mupirocin (2%) nasal ointment 3 times/day x 7 days	Neomycin sulphate (0.1%) nasal ointment 3 times/day x 7 days	3	None
Sesso et al 1994	22	Randomised controlled clinical trial	Teaching hospital	CAPD patients >15 years, 23% diabetic	Sodium fusidate (2%) nasal ointment 2 times/day x 5 days, every 1 month	Placebo	7	Trial with 3 arms, including oral ofloxacin 200 mg/day x 5 days versus placebo versus nasal sodium fusidate

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)		
Bernardini et al 1996	Unclear	No	No	No	Yes	0
Mupirocin Study Group 1996	Unclear	Yes	Yes	No	No	0
Perez Fontan et al 1992	Unclear	No	No	No	No	13.6
Sesso et al 1994	Unclear	No	No	No	No	0

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]
Bernardini et al 1996	Rate of S. aureus catheter infection	Not estimable (0-61 episodes/dialysis year)┼	Not estimable (0-42 episodes/dialysis year)	Not estimable	Not estimable
Mupirocin Study Group 1996	Peritonitis	43/134	44/133	0.97 (0.69 to 1.37)	-0.01 (-0.12 to 0.10)
	Peritonitis rate*	18/1390	19/1236	0.84 (0.44 to 1.60)	0.00 (-0.01 to 0.01)
	Exit-site/tunnel infection	26/134	25/133	1.03 (0.63 to 1.69)	0.01 (-0.09 to 0.10)
	Exit-site/tunnel infection rate*	42/1390	64/1236	0.58 (0.40 to 0.85)	-0.02 (-0.04 to -0.01)
	All-cause mortality	22/134	25/133	0.87 (0.52 to 1.47)	-0.02 (-0.12 to 0.07)
Perez Fontan et al 1992	Peritonitis rate*	5/133	4/76	0.71 (0.20 to 2.58)	-0.02 (-0.07 to 0.04)
Sesso et al 1994	Peritonitis	1/9	5/13	0.29 (0.04 to 2.07)	-0.27 (-0.61 to 0.06)
	Exit-site/tunnel infection	5/9	3/13	2.41 (0.76 to 7.62)	0.32 (-0.07 to 0.72)
	Catheter removal	4/9	6/13	0.96 (0.38 to 2.46)	-0.02 (-0.44 to 0.41)
	All-cause mortality	0/9	1/13	0.47 (0.02 to 10.32)	-0.17 (-0.40 to 0.07)

*Given as episodes/total patient months on PD
┼NA = not available