Nephrol Dial Transplant (2002) 17: 1802–1807

Nephrology Dialysis Transplantation

Original Article

A randomized controlled trial of topical exit site mupirocin application in patients with tunnelled, cuffed haemodialysis catheters

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Abstract

Background. Central venous catheters are frequently needed for the provision of haemodialysis, but their clinical usefulness is severely limited by infectious complications. The risk of such infections can be reduced by topical application of mupirocin to the exit sites of non-cuffed catheters or by the use of tunnelled, cuffed catheters. Whether mupirocin offers any additional protection against infection in patients with tunnelled, cuffed haemodialysis catheters has not been studied.

Methods. An open-label, randomized controlled trial was performed comparing the effect of thrice-weekly exit site application of mupirocin (mupirocin group) *vs* no ointment (control group) on infection rates and catheter survival in patients receiving haemodialysis via a newly inserted, tunnelled, cuffed central venous catheter. All patients were followed until catheter removal and were monitored for the development of exit site infections and catheter-associated bacteraemias.

Results. Fifty patients were enrolled in the study. Both the mupirocin ($n=27$) and control ($n=23$) groups were similar at baseline with respect to demographic characteristics, comorbid illnesses and causes of renal failure. Compared with controls, mupirocin-treated patients experienced significantly fewer catheter-related bacteraemias (7 *vs* 35%, $P<0.01$) and a longer time to first bacteraemia (log rank score 8.68, $P<0.01$). The beneficial effect of mupirocin was entirely attributable to a reduction in staphylococcal infection (log rank 10.69, $P=0.001$) and was still observed when only patients without prior nasal *Staphylococcus aureus* carriage were included in the analysis (log rank score 6.33, $P=0.01$). Median catheter survival was also significantly longer in the mupirocin group (108 *vs* 31 days, log rank score 5.9, $P<0.05$). Mupirocin use was not associated with any adverse patient effects or the induction of antimicrobial resistance.

Conclusions. Thrice-weekly application of mupirocin to tunnelled, cuffed haemodialysis catheter exit sites is associated with a marked reduction in line-related sepsis and a prolongation of catheter survival.

Keywords: antibiotics therapeutic use; bacteraemia; catheterization, central venous; dialysis; equipment contamination; staphylococcal infections

Introduction

Central venous catheterization is an established method of providing rapid, temporary access for the provision of haemodialysis to patients with serious acute or chronic renal failure. Unfortunately, the clinical usefulness of this method is severely limited by the frequent occurrence of bloodstream infections in up to 40% of cases [1–7]. A number of randomized controlled trials have convincingly demonstrated that tunnelled, cuffed catheters are associated with a much lower risk of bacterial colonization, exit site infection, and bacteraemia compared with non-tunnelled and non-cuffed devices [1,6,8,9]. The protective effect of tunnelling and cuffing is postulated to be due to a combination of prevention of bacterial migration along the sinus tract and provision of more effective catheter anchorage and immobilization [7].

Catheter-associated infection rates have also recently been shown to be significantly reduced by regular topical application of mupirocin to the exit sites of non-cuffed, non-tunnelled haemodialysis cannulae [2,10]. Mupirocin is an antibiotic with activity against Gram-positive organisms and is thought to reduce device-related infections by preventing staphylococcal exit site colonization [10]. There have been no studies on the use of mupirocin in combination with

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tunnelled, cuffed catheters and it is, therefore, uncertain whether a further reduction in infection rates would be achieved beyond that afforded by tunnelled, cuffed catheters alone. Moreover, the regular use of mupirocin is not without risk, as it has been shown by some authors to be associated with the appearance of resistant staphylococcal strains [11,12].

The aim of the present study was to determine the safety and efficacy of topical exit site application of mupirocin in preventing infections secondary to tunnelled, cuffed haemodialysis catheters.

Subjects and methods

Study population

All adult patients with acute or chronic renal failure who required haemodialysis via a newly inserted tunnelled, cuffed central venous catheter at the Princess Alexandra Hospital were invited to participate in the study. Informed consent was obtained from all patients prior to their inclusion in the trial and the study protocol was reviewed and approved by the Princess Alexandra Hospital Research Ethics Committee.

Study design

The study was a prospective, open-label, randomized, controlled trial. Patients who were enrolled in the study were randomly assigned to receive either topical 2% calcium mupirocin ointment (Bactroban, SmithKline Beecham Pharmaceuticals, Australia; mupirocin group) or no ointment (control group) in addition to standard exit site care and 10% povidone iodine disinfection. The randomization was performed using sequentially numbered, opaque, sealed envelopes. The sequence of interventions was obtained from a computer-generated random number list.

All patients underwent ultrasound-guided placement of a subcutaneously tunnelled, internal jugular venous haemodialysis catheter (PermCath, Quinton Instrument Company, Seattle, WA, USA) by dedicated vascular access surgeons according to the method described by Schwab *et al.* [7]. Prophylactic pre-operative antibiotics were not prescribed. All catheters received 10% povidone iodine disinfection at the site of insertion and were covered by an opaque, air-permeable, non-woven fabric dressing (Primapore, Smith & Nephew, Sydney, Australia). Chest radiographs were obtained after insertion to confirm the position of the catheter tip in the superior vena cava. Central venous catheters were dedicated to haemodialysis use and were not accessed for other purposes. Subsequent catheter site care was performed by trained haemodialysis registered nurses using a rigorous aseptic technique. Primapore dressings were changed thrice-weekly at each haemodialysis treatment and the sites were recleansed with 10% povidone iodine solution. Patients allocated to the mupirocin group additionally received approximately 10 mm of mupirocin ointment squeezed directly on to their exit sites from a 15 g tube with an outlet diameter of 5 mm. At the completion of each haemodialysis treatment, sodium heparin (1000 U/ml) was injected into each lumen in a volume equivalent to the priming volume of the catheter.

At the time of inclusion in the study, demographic and clinical data were recorded. Patients had their anterior nares cultured for *Staphylococcus aureus*, but identified nasal carriers were not treated. Patients were followed up until the catheter was removed. The primary outcome measures were exit site infection, catheter-related bacteraemia and adverse reactions (primarily mupirocin resistance amongst staphylococcal isolates).

Definitions

Catheter-related infections were defined according to standard guidelines [1,13,14]. Exit site infection was defined as purulent exit site discharge or two out of three of exit site eythema, tenderness and induration with a positive culture. Catheter-associated bacteraemia was defined as either: (i) a single positive blood culture together with a positive culture of the catheter tip or exit site with an identical organism, or (ii) two or more positive blood cultures (or a single positive blood culture for *S. aureus*) with no evidence of infection source other than the device.

Microbiology

Exit site swabs were obtained using sterile, premoistened calcium alginate swabs in all suspected cases of exit site infection (erythema, tenderness, induration, or discharge). The swabs were streaked onto plates containing blood agar, colistin-nalidixic acid agar, McConkey's media, and mannitol-salt agar. All cultures were incubated at 35°C for 48 h and examined daily for growth. Patients with suspected bacteraemia (fever greater than 38°C, rigors, leukocytosis, or clinically unwell) were investigated with exit swabs and at least two sets of blood cultures (20 ml). Staphylococcal isolates were routinely screened for mupirocin resistance by agar dilution in which samples were streaked on plates containing 1 mg/ml mupirocin. The microbiologists processing the specimens were blinded to the patient's allocation group.

In cases of probable or definite catheter-associated bacteraemia, the catheter was removed and the tip sent for microbiologic culture. Approximately 50 mm of catheter tip was rolled across chocolate agar plates and processed according to the semiquantitative method of Maki *et al.* [14]. Catheter colonization was defined as the recovery of greater than 15 colony-forming units.

Statistical analysis

Normality of data was evaluated by the Kolmogorov–Smirnov test with Lilliefor's correction. Results are expressed as mean $\pm$ SEM for continuous parametric data, median (interquartile range) for continuous non-parametric data, and frequencies and percentages for categorical data. Comparisons between the control and mupirocin groups were performed using Student's *t*-test or the Mann–Whitney *U* test, depending on data distribution. Differences in proportions were evaluated by χ^2 or Fisher's exact tests. Infection-free survival curves, survival probabilities, and estimated mean survival times were generated according to the Kaplan–Meier method. Differences in the survival curves between the two groups were evaluated using the log rank test. A multivariate Cox's proportional hazards model was also applied, which included mupirocin administration, age, sex, race, body mass index, diabetic status, prior immunosuppression, acuity of renal failure, and serum albumin as covariates. All data were analysed on an intention-to-treat basis using the statistical software package SPSS release

Table 1. Baseline patient characteristics

Characteristic	Control ($n=23$)	Mupirocin ($n=27$)
Age (years)	56.6 ± 2.9	53.8 ± 3.6
Female sex	61%	44%
Caucasoid race	83%	89%
Body mass index (kg/m^2)	26.4 ± 1.4	28.6 ± 1.7
Serum albumin (g/l)	31.8 ± 0.8	31.9 ± 0.8
Serum ferritin (μg/l)	322 ± 59	343 ± 51
Diabetes mellitus	43%	37%
Symptomatic vascular disease	48%	41%
Prior immunosuppression	22%	22%
Prior catheter use	13%	11%
Nasal staphylococcal carriage	26%	22%
Catheter indication		
Acute temporary dialysis	22%	19%
Commencing chronic dialysis	26%	32%
Clotted vascular access	26%	19%
Failed peritoneal dialysis	25%	26%
Permanent access	0%	4%

None of the differences between the groups was statistically different.

version 10.0.5 (SPSS Inc., Chicago, IL, USA). *P* values less than 0.05 were considered significant.

Power calculations for the infection-free survival analyses were performed using the software package PS version 1.0.17 (Vanderbilt University Medical Center, Nashville, TN, USA). It was estimated that the study had adequate statistical power (90% probability) to detect at least a doubling in mean catheter-associated infection-free survival from a control level of 50 days, assuming $\alpha = 0.05$, if 46 patients were recruited in the study (23 in each group).

Results

Patient characteristics

A total of 50 patients required insertion of tunnelled, cuffed central venous catheters for the provision of haemodialysis at the Princess Alexandra Hospital between 1 August 1999 and 31 May 2001. All patients agreed to participate in the study and none were lost to follow-up. Twenty-three patients were randomly allocated to the control group, whilst 27 patients received mupirocin. There were no significant differences between the two groups with respect to their baseline characteristics (Table 1).

Exit site infections

Exit site infections were observed in five controls (6.6 episodes per 1000 catheter-days) and no mupirocin-treated patients ($P<0.05$). The time to first exit site infection was significantly shorter in the control group than in the mupirocin group (log rank 7.3, $P<0.01$) (Figure 1). The organisms responsible for exit site infection in the control group were *S. aureus* ($n=4$) and *Pseudomonas aeruginosa* ($n=1$). Four of the five exit site infections (80%) were accompanied by bacteraemia.

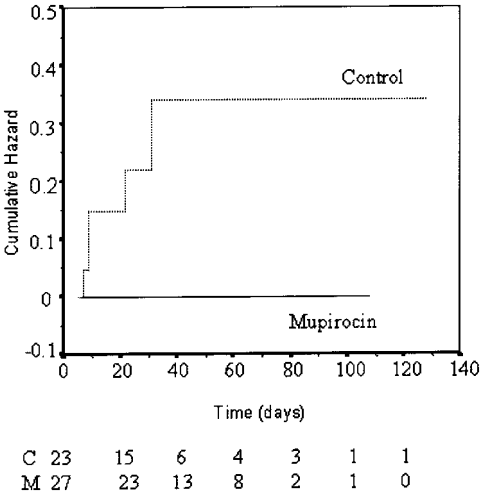

Fig. 1. Cumulative hazard plot of exit site infections. The difference between the mupirocin and control groups was statistically significant (log rank score 7.3, $P<0.01$). The number of patients at risk within each group is indicated beneath the corresponding time periods on the *x*-axis.

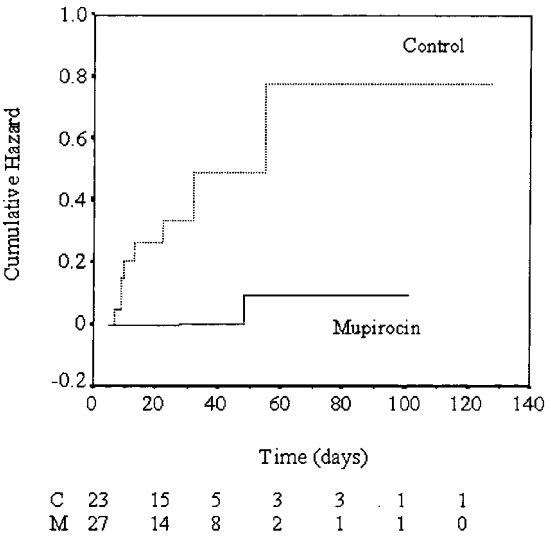

Fig. 2. Cumulative hazard plot of catheter-associated bacteraemias. The difference between the mupirocin and control groups was statistically significant (log rank score 7.0, $P<0.01$). The number of patients at risk within each group is indicated beneath the corresponding time periods on the *x*-axis.

Bacteraemia

Catheter-associated bacteraemias were observed more frequently in controls ($n=8$, 35%) than in mupirocin-treated patients ($n=2$, 7%, $P<0.01$). The incidences of bacteraemia were 10.5 and 1.6 episodes per 1000 catheter-days, respectively. Mupirocin treatment was associated with an odds ratio for bacteraemia of 0.15 (95% CI 0.03–0.80). The number needed to be treated with mupirocin to prevent one episode of bacteraemia was 3.7. Mupirocin significantly increased the median bacteraemia-free survival from 55 to 108 days (log rank score 7.0, $P<0.01$) (Figure 2). *Staphylococcus aureus* septicaemia accounted for half of the bacteraemias in the controls ($n=4$), but was not observed

in mupirocin-treated patients ($n=0$). The other organisms identified in the control group included *Enterobacter cloacae* ($n=1$), *Enterobacter aerogenes* ($n=1$), *P. aeruginosa* ($n=1$), and *Staphylococcus epidermidis* ($n=1$), whilst the organisms in the mupirocin group were *P. aeruginosa* ($n=1$) and a *Rhodococcus* species ($n=1$). Exit site infections accompanied half of the bacteraemic episodes in controls, but none of the episodes in mupirocin-treated patients.

When the results for bacteraemias and exit site infections were combined, median infection-free survival was significantly increased in the mupirocin group (108 *vs* 55 days, log rank score 8.7, $P<0.01$). One episode of catheter-associated infection was prevented for every 3.1 patients treated with mupirocin. On multivariate Cox proportional hazards model analysis, mupirocin administration was a significant predictor of infection-free survival (adjusted hazard ratio 0.02, 95% CI 0.00–0.39, $P<0.01$) independent of age, sex, race, body mass index, diabetic status, prior immunosuppression, acuity of renal failure, and serum albumin. The improved infection-free survival was primarily explained by a reduction in staphylococcal infection (log rank score 10.7, $P=0.001$). The occurrence of non-staphylococcal infection was not different between the two groups (log rank score 0.7, $P=0.4$).

Twelve patients harboured *S. aureus* in their anterior nares at the commencement of the study (six in each group). Mupirocin use tended to be associated with a reduced occurrence of catheter-related sepsis in nasal staphylococcal carriers (0% mupirocin *vs* 50% controls, $P=0.09$) and with a prolonged time to first infection (log rank score 3.2, $P=0.07$). Patients who did not have nasal colonization with staphylococci at baseline exhibited a lower frequency of catheter-associated infection (10 *vs* 26%, $P=0.06$) and a significantly increased time to first infection (log rank score 6.3, $P=0.01$) if they were allocated to the mupirocin rather than control groups.

Catheter survival

Tunnelled, cuffed central venous catheters were removed prematurely in 13 (57%) controls and five (19%) mupirocin-treated patients ($P<0.01$, odds ratio 0.18 mupirocin *vs* controls, 95% CI 0.05–0.63). The median catheter survivals, censored for end of treatment, in the control and mupirocin groups were 31 and 108 days, respectively (log rank score 5.9, $P<0.05$) (Figure 3). Infection was the major reason for premature removal (39 *vs* 7%, respectively, $P<0.01$). The other reasons for removal included catheter thrombosis (9 *vs* 7%, $P=$NS), cracking (4 *vs* 0%, $P=$NS), and inadvertent patient removal (4 *vs* 4%, $P=$NS).

Adverse reactions and costs

No local or systemic adverse reactions to mupirocin ointment were observed during the period of the study. Mupirocin-resistant staphylococcal isolates were not detected.

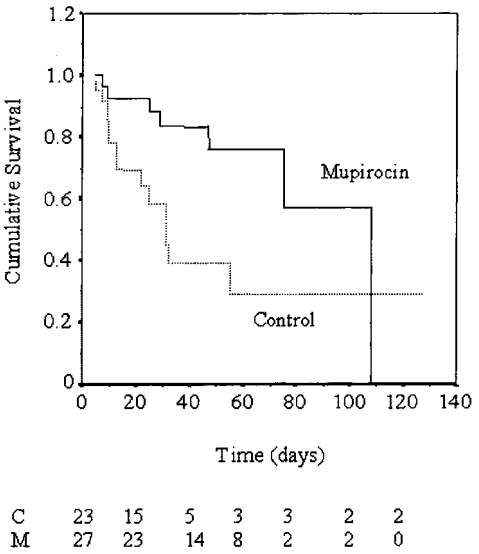

Fig. 3. Kaplan–Meier curve for catheter survival. The difference between the mupirocin and control groups was statistically significant (log rank score 5.9, $P<0.05$). The number of patients at risk within each group is indicated beneath the corresponding time periods on the *x*-axis.

The median cost of exit site application for the average life of a catheter was $7.50 US per patient. This compared favourably with the median costs of reinserting a new tunnelled, cuffed catheter following premature catheter removal (catheter, surgeon/anaesthetist/theatre fees, fluoroscopy—$824 US per catheter) and therapy for catheter-related septicaemia (hospitalization, medications, investigation—$1744 US per episode).

Discussion

The present study demonstrated for the first time that regular, three times a week, topical exit site application of 2% calcium mupirocin ointment was safe and substantially reduced the risk of catheter-related infections and premature catheter removal in patients with tunnelled, cuffed haemodialysis catheters. This benefit was entirely explained by a reduction in staphylococcal infection rates and was able to be demonstrated even in patients who were not nasal carriers of *S. aureus* at the time of catheter insertion.

Our results are similar to a previous study by Sesso *et al.* [2] involving chronic renal failure patients with non-cuffed, non-tunnelled haemodialysis catheters in whom topical mupirocin prophylaxis reduced *S. aureus* bacteraemia rates from 8.9 to 0.7 episodes per 1000 patient-days. Unfortunately, a significant limitation of that study was the applicability of their findings to patients with tunnelled, cuffed catheters. Numerous randomized controlled trials [6,8,9] and a meta-analysis [1] have clearly demonstrated that cuffing and tunnelling of central venous catheters result in a significant 44–77% reduction in the risk of catheter-related sepsis compared with catheters that

are not cuffed or tunnelled. This risk reduction may occur as a result of both improved catheter stability and impeded migration of bacteria from the cutaneous exit site to the venous entry site. Although such an effect could potentially have negated the beneficial impact of mupirocin on catheter-related sepsis, our study has clearly demonstrated that this is not the case.

Mupirocin also conferred considerable protection against bacteraemia in patients who were not nasal carriers of *S. aureus*, with one episode prevented for every 6.7 such patients treated. Nasal staphylococcal colonization has been shown to be associated with at least a 3-fold increased risk of *S. aureus* infection in both haemodialysis and peritoneal dialysis patients [4]. Moreover, eradication of nasal carriage by local mupirocin application was reported in one study of chronic haemodialysis patients to promote a 4-fold reduction in *S. aureus* bacteraemia compared with historical controls [4]. In the present study, the odds ratio for staphylococcal infections in patients who were not nasal carriers was 0.26. Despite their lower risk of staphylococcal sepsis, mupirocin prophylaxis was still effective in this population.

The incidence of catheter-related bacteraemia in the study control group (10.5 episodes/1000 catheter-days) was somewhat higher than has been reported in other series [3,5,7,15–17], where the observed occurrence rates have ranged between 1.0 and 5.5 episodes/1000 catheter-days. This may have been related to the fact that the study was performed in sub-tropical conditions and included a larger number of 'high-risk' patients, such as those with diabetes mellitus (44%), recent ($\leqslant$1 month) infections (24%), acute renal failure (20%), nasal staphylococcal carriage (24%), and recent immunosuppressive therapy (22%). In addition, the relatively prompt removal of uninfected catheters in our study due to early completion of temporary access therapy (i.e. maturation of permanent vascular access or recovery of acute renal failure) would have tended to relatively inflate our infection rate, when expressed per 1000 catheter-days, due to the fact that catheter-associated infections are more likely to occur shortly after catheter insertion. Thus, when catheter-associated bacteraemias were alternatively expressed as time to first episode, the median time interval between catheter insertion and onset of infection in our control patients (55 days) was comparable with that reported by Beathard [16] (62 days), despite a sizeable observed variation in bacteraemic episodes per 1000 catheter-days (10.5 *vs* 3.4, respectively). The similarity in reported infection-free survival between our control patients and this recent, large series of haemodialysis patients with tunnelled, cuffed catheters suggests that the results obtained with topical mupirocin prophylaxis should be generalizable to other dialysis units.

Two potential weaknesses of the trial were its open-label design and the failure to use placebo ointment in the control group. Placebo ointment was intentionally avoided because it was reasoned that such a preparation may have promoted infection by providing a favourable culture medium, thereby necessitating an additional (untreated) control group and decreasing the feasibility of performing the study. The subsequent lack of blinding could have potentially introduced co-intervention and observer bias. For example, Wagman *et al.* [18] showed an 8-fold higher rate of infections associated with tunnelled, cuffed catheters managed outside study protocol compared with those managed using the technique required by the study. Such protocol deviations were strictly avoided in the present study by ensuring that nursing staff adhered to a standardized exit site care protocol and carefully documented their actions at each dressing change. Moreover, observer bias was minimized by the use of clearly defined, objective outcome measures and by blinding microbiology laboratory staff processing culture samples to the patient's study group assignment.

This study has important implications for the management of haemodialysis patients with temporary haemodialysis catheters. Such patients account for 6% of all haemodialysis patients in Australia [19] and are at great risk of morbidity and mortality from catheter-related sepsis. Although some papers have reported the development of mupirocin resistance following routine prophylactic use of this antimicrobial agent, particularly for dermatologic indications [12], most studies [20], including ours, have not found antimicrobial resistance to be a significant problem in dialysis populations. Nevertheless, routine surveillance of staphylococcal isolates for mupirocin resistance would be prudent in units where topical mupirocin prophylaxis is employed.

In conclusion, the present investigation demonstrated that the application of 2% calcium mupirocin ointment to the exit sites of tunnelled, cuffed haemodialysis catheters, in addition to standard disinfection with 10% povidone iodine, significantly prolonged catheter survival and reduced the incidence of exit site infection and catheter-associated bloodstream infection. The reduction in device-related sepsis was due to a decreased risk of *S. aureus* infection, whilst the risk of non-staphylococcal infection was unaltered. The benefit of mupirocin prophylaxis was not restricted to nasal carriers of *S. aureus*. Although additional studies are warranted to confirm these findings, mupirocin chemoprophylaxis appears to be a safe and highly cost-effective infection control strategy in patients with tunnelled, cuffed haemodialysis catheters.

References

1. Randolph AG, Cook DJ, Gonzales CA, Brun-Buisson C. Tunneling short-term central venous catheters to prevent catheter-related infection: a meta-analysis of randomized, controlled trials. *Crit Care Med* 1998; 26: 1452–1457
2. Sesso R, Barbosa D, Leme IL *et al. Staphylococcus aureus* prophylaxis in hemodialysis patients using central venous catheter: effect of mupirocin ointment. *J Am Soc Nephrol* 1998; 9: 1085–1092
3. Swartz RD, Messana JM, Boyer CJ *et al.* Successful use of cuffed central venous hemodialysis catheters inserted percutaneously. *J Am Soc Nephrol* 1994; 4: 1719–1725

4. Boelaert JR, Van Landuyt HW, Godard CA *et al*. Nasal mupirocin ointment decreases the incidence of *Staphylococcus aureus* bacteraemias in haemodialysis patients. *Nephrol Dial Transplant* 1993; 8: 235–239
5. Moss AH, Vasilakis C, Holley JL *et al*. Use of a silicone dual-lumen catheter with a Dacron cuff as a long-term vascular access for hemodialysis patients. *Am J Kidney Dis* 1990; 16: 211–215
6. Flowers RH, Schwenzer KJ, Kopel RF *et al*. Efficacy of an attachable subcutaneous cuff for the prevention of intravascular catheter-related infection. A randomized, controlled trial. *J Am Med Assoc* 1989; 261: 878–883
7. Schwab SJ, Buller GL, McCann RL, Bollinger RR, Stickel DL. Prospective evaluation of a Dacron cuffed hemodialysis catheter for prolonged use. *Am J Kidney Dis* 1988; 11: 166–169
8. Timsit JF, Sebille V, Farkas JC *et al*. Effect of subcutaneous tunneling on internal jugular catheter-related sepsis in critically ill patients: a prospective randomized multicenter study. *J Am Med Assoc* 1996; 276: 1416–1420
9. Keohane PP, Jones BJ, Attrill H *et al*. Effect of catheter tunnelling and a nutrition nurse on catheter sepsis during parenteral nutrition. A controlled trial. *Lancet* 1983; 2: 1388–1390
10. Hill RL, Fisher AP, Ware RJ, Wilson S, Casewell MW. Mupirocin for the reduction of colonization of internal jugular cannulae—a randomized controlled trial. *J Hosp Infect* 1990; 15: 311–321
11. Hill RL, Casewell MW. Nasal carriage of MRSA: the role of mupirocin and outlook for resistance. *Drugs Exp Clin Res* 1990; 16: 397–402
12. Cookson BD, Lacey RW, Noble WC *et al*. Mupirocin-resistant *Staphylococcus aureus*. *Lancet* 1990; 335: 1095–1096
13. Bureau of Infectious Diseases Division of Nosocomial and Occupational Infections. Infection control guidelines: preventing infections associated with indwelling intravascular access devices. *Health Canada* 1997; 23: S8–S11
14. Maki DG, Weise CE, Sarafin HW. A semiquantitative culture method for identifying intravenous-catheter-related infection. *N Engl J Med* 1977; 296: 1305–1309
15. Nassar GM, Ayus JC. Infectious complications of the hemodialysis access. *Kidney Int* 2001; 60: 1–13
16. Beathard GA. Management of bacteremia associated with tunneled-cuffed hemodialysis catheters. *J Am Soc Nephrol* 1999; 10: 1045–1049
17. Saad TF. Bacteremia associated with tunneled, cuffed hemodialysis catheters. *Am J Kidney Dis* 1999; 34: 1114–1124
18. Wagman LD, Kirkemo A, Johnston MR. Venous access: a prospective, randomized study of the Hickman catheter. *Surgery* 1984; 95: 303–308
19. Disney APS, Russ GR, Walker R *et al*. ANZDATA Registry Report 2000. Australia and New Zealand Dialysis and Transplant Registry, Adelaide, South Australia, 2000
20. Kluytmans JA, Manders MJ, van Bommel E, Verbrugh H. Elimination of nasal carriage of *Staphylococcus aureus* in hemodialysis patients. *Infect Control Hosp Epidemiol* 1996; 17: 793–797

Received for publication: 4.3.02
Accepted in revised form: 17.5.02