EXIT-SITE DRESSING AND INFECTION IN PERITONEAL DIALYSIS: A RANDOMIZED CONTROLLED PILOT TRIAL

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◆ **Objective:** Peritoneal dialysis (PD)-related infection is a common cause of catheter loss and the main reason for PD drop-out. Exit-site infection (ESI) is a pathway to developing tunnel infection and peritonitis, hence rigorous exit-site care has always been emphasized in PD therapy. The aim of this study was to evaluate the effect of exit-site dressing vs non-dressing on the rate of PD-related infection.

◆ **Methods:** A prospective randomized controlled study was conducted in prevalent PD patients at the Hospital Tuanku Jaafar Seremban, Negeri Sembilan, Malaysia, from April 2011 until April 2013. All patients were required to perform daily washing of the exit site with antibacterial soap during a shower. In the dressing group ($n=54$), patients were required to clean their exit site using povidone-iodine after drying, followed by topical mupirocin antibiotic application to the exit site. The exit site was then covered with a sterile gauze dressing and the catheter immobilized with tape. In the non-dressing group ($n=54$), patients were not required to do any further dressing after drying. They were only required to apply mupirocin cream to the exit site and then left the exit site uncovered. The catheter was immobilized with tape. The primary outcome was ESI. The secondary outcomes were evidence of tunnel infection or peritonitis.

◆ **Results:** A total of 97 patients completed the study. There were a total of 12 ESI episodes: 4 episodes in 4 patients in the dressing group vs 8 episodes in 4 patients in the non-dressing group. This corresponds to 1 episode per 241.3 patient-months vs 1 episode per 111.1 patient-months in the dressing and non-dressing groups respectively. Median time to first ESI episode was shorter in the non-dressing than in the dressing group, but not significant ($p=0.25$). The incidence of gram-positive ESI in both groups was similar. There were no gram-negative ESI in the non-dressing group compared with 2 in the dressing group.

The peritonitis rate was 1 per 37.1 patient-month in the dressing group and 1 per 44.4 patient-months in the non-dressing group. Median time to first peritonitis episode was significantly shorter in the dressing group compared to non-dressing ($p=0.03$). There was no impact of dressing disruptions in the occurrence of major PD catheter-related infection.

◆ **Conclusion:** Use of a non-dressing technique with only prophylactic topical mupirocin cream application is effective in preventing PD-related infection. The non-dressing technique is more cost-effective and convenient for PD patients, with fewer disposables.

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KEY WORDS: Dressings; exit-site infection; tunnel infection; peritonitis.

Peritoneal dialysis (PD)-related infection is a common cause of catheter loss (1,2), and accounts for 14% of the PD technique failure in Malaysia (3). Prevention of PD infection is an integral part of and a prerequisite for successful maintenance of PD therapy. Exit-site infections (ESIs) have been shown to have a significant impact on PD complications. Exit-site infection is the pathway to developing subsequent tunnel infection and peritonitis (4) that leads to high rates of catheter loss, morbidity, and mortality (5–8).

Exit-site infections are caused by touch contamination organisms, especially gram-positive *S. aureus* (9,10) and gram-negative *P. aeruginosa* (11). Infection with *S. aureus* and *P. aeruginosa* is a major challenge in PD therapy, with high rates of catheter loss, hospitalization, and peritoneal membrane failure, and also may lead to death (12). The Malaysian National Renal Registry 2012 (3) reported that gram-positive organisms accounted for 36% of peritonitis episodes, with *S. aureus* as the predominant organism, whereas 9% of gram-negative peritonitis episodes are due to *P. aeruginosa*. Many different rigorous exit-site dressing protocols have been proposed as a preventive measure to decrease infections by these organisms (13–19). According to the Malaysian Ministry of Health, the total cost of an exit-site dressing set is MYR 1200.50 (USD 375.20) per patient per year.

Interventions for exit-site care involve antiseptics, antimicrobial products, and application of cover dressings to assist in maintaining an infection-free exit site. The International Society for Peritoneal Dialysis (ISPD) recommends implementing exit-site dressing immediately post-operatively and at least daily or on alternate days after completing training (13).

Different cleansing agents for exit-site care with either povidone iodine or antibacterial soap have been studied, with conflicting results (15,16,20–22). Gauze and semi-permeable or occlusive dressings have been used to keep the exit site clean, protect it from trauma, and also to anchor the catheter. Topical antibiotic application at the exit site has been shown to reduce the risk of ESI. For example, mupirocin cream is associated with

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a significantly lower risk of *S. aureus* infection (17–19). However, there has been the emergence of mupirocin cream-resistant *S. aureus* (23,24), and the cream is less effective in the prevention of *P. aeruginosa* infection. In contrast, gentamicin cream has been shown to be as effective as mupirocin and reduces the risk of both *S. aureus* and *P. aeruginosa* infection (25).

The aim of this study was to evaluate the effect of exit-site dressing vs non-dressing on the rate of exit-site infection and, secondarily, the rates of tunnel infection and peritonitis.

METHODS

STUDY DESIGN AND PARTICIPANTS

A prospective randomized controlled study was conducted in prevalent PD patients at the Hospital Tuanku Jaafar Seremban, Negeri Sembilan, Malaysia, from April 2011 until April 2013. Permission was obtained from the Malaysian Human Research Ethics Committee. The study was conducted in accordance with the Declaration of Helsinki, the International Conference and Harmonization Guidelines for Good Clinical Practice and the National Medical Research Registry (NMRR-13-857-14821). Informed consent was obtained from all participants by the attending physician.

Patients who were ≥ 18 years old and had been on PD for more than 3 months were included in the study. Patients with an exposed external cuff and those with a recent episode of ESI, tunnel infection or peritonitis in the previous 30 days were excluded.

Patients were allocated into 2 groups (1:1 ratio) by block randomization. The treatment allocation was not blinded. All patients were required to expose their exit site and perform daily washing of the exit site with antibacterial soap during a shower. This was followed by thorough drying of the exit site by patting dry with a clean towel.

In the dressing group, patients were required to clean their exit site using povidone-iodine after drying, followed by topical mupirocin antibiotic application to the exit site. The exit site was then covered with a sterile gauze dressing and the catheter immobilized with tape.

In the non-dressing group, patients were not required to do any further dressing after drying. They were only required to apply mupirocin cream to the exit site and then left the exit site uncovered. The catheter was immobilized with tape. During the study period, nasal mupirocin eradication was not practiced routinely unless *S. aureus* was isolated from the exit site.

OUTCOME MEASURES

The primary outcome was ESI. The secondary outcomes were evidence of tunnel infection or peritonitis.

Demographic data and clinical records were reviewed. Each patient was followed up at 3-month intervals in the clinic for 24 months. The PD nurse examined the exit site during each clinic visit for any evidence of PD-related infection (ESI, tunnel infection, or peritonitis). Patients were required to notify the

PD nurse by telephone and come to the PD unit immediately if any evidence of PD-related infection occurred between the clinic visits.

Exit-site infection was defined as purulent discharge, with or without erythema of the skin at the catheter-epidermal interface. A tunnel infection may present as erythema, edema or tenderness over the subcutaneous pathway. Cultures from exit sites were obtained from drainage if present. Peritonitis was defined as cloudy fluid PD effluent with white cell count > 100 cells/ μ l and presence of $\geq 50\%$ polymorphonuclear cells. Cultures of PD effluent were obtained using blood culture bottles. Infections were treated accordingly with antibiotics by the nephrologists. Catheters were removed if ESI, tunnel infection, or peritonitis did not improve with medical treatment.

STATISTICAL ANALYSIS

Data were expressed as means and standard deviation (SD) or medians. An independent *t*-test was used to compare the 2 groups. A Mann-Whitney analysis was done if the assumption of normal distribution was not met for the *t*-test. A Chi-square test was used to compare differences for categorical data between groups and Fisher's exact test was used if the assumption for Chi-square was not met.

The IBM SPSS Statistics for Windows software (Version 20.0, IBM Corp, Armonk, NY, USA) was used for the statistical analysis, and *p* values less than 0.05 were considered significant.

RESULTS

PATIENT CHARACTERISTICS

The average age of the study participants was 50.6 years in the dressing group and 52.4 years in the non-dressing group (Table 1). More than half of the patients in both groups had diabetes. There was no significant difference between the groups in terms of PD treatment duration. The median follow-up duration was 639 days (interquartile range [IQR] = 45) in the dressing group and 627 days (IQR = 86) days in the non-dressing group.

Care assistance from family members was required by 23.5% and 16.3% of patients in the dressing and non-dressing groups, respectively. A total of 97 patients (90.7%) completed the study. Six patients died, 4 patients transferred to hemodialysis (Figure 1).

PRIMARY OUTCOME

Overall, ESI in our study was low. There were 4 episodes of ESI in 4 (8.1%) patients in the dressing group vs 8 episodes of ESI in 4 (8.3%) patients in the non-dressing. This corresponds to 1 episode per 241.3 patient-months in the dressing group and 1 episode per 111.1 patient-months in the non-dressing group. The median time to the first ESI episode was shorter in the non-dressing group than in the dressing group but not significantly (*p* = 0.25) (Table 2). All the ESI episodes responded well to antibiotic therapy.

TABLE 1
Patient Characteristics

	Dressing (n=49)	Non-dressing (n=48)	p value
Mean age, years±SD	50.6±16.14	52.4±14.41	0.55
Gender, n (%)			0.69
Male	23 (45.1%)	24 (49%)	
Female	28 (54.9%)	25 (51%)	
Assisted care, n (%)	12 (23.5%)	8 (16.3%)	0.52
Diabetes, n (%)	35 (68.6%)	38 (77.6%)	0.44
Median days on PD before recruitment, (IQR)	407 (567)	248 (654)	0.24
Median follow-up, days (IQR)	639 (45)	627 (86)	0.18

SD = standard deviation; PD = peritoneal dialysis; IQR = interquartile range.

Figure 1 — Patient flowchart. PD = peritoneal dialysis; HD = hemodialysis.

In the dressing group, organisms isolated from the ESI were *S. aureus* (1 patient), *P. aeruginosa* (2 patients), and coagulase-negative *Staphylococcus* (1 patient). In the non-dressing group, the organisms isolated were *S. aureus* (1 patient), coagulase-negative *Staphylococcus* (2 patients), diphtheroid (1 patient), and 4 culture-negative.

SECONDARY OUTCOME MEASURES

There was only 1 tunnel infection during the study period. This was observed in the non-dressing group.

There were a total of 46 episodes of peritonitis in 97 PD patients: 26 (56.5%) patients in the dressing group vs 20

TABLE 2
Exit-Site and Peritoneal Infections

	Dressing (n=49)	Non-dressing (n=48)	p value
Exit-site infection organism			
Gram-positive bacteria			
<i>S. aureus</i>	1	1	
Other gram-positive	1	3	
Gram-negative bacteria			
<i>Pseudomonas aeruginosa</i>	2	0	
Other gram-negative	0	0	
Yeast	0	0	
Culture-negative	0	4	
Others	0	0	
ESI rate (patient-months per episode)	1:241.3	1:111.1	
Median time to first ESI, days (IQR)	177.5 (317.5)	85.0 (110.5)	0.25
Peritonitis organism			
Gram-positive bacteria			
<i>S. aureus</i>	1	0	
Other gram-positive	4	0	
Gram-negative bacteria			
<i>Pseudomonas aeruginosa</i>	1	1	
Other gram-negative	9	10	
Yeast	1	0	
Culture-negative	6	7	
Others	4	2	
Peritonitis rate (patient- months per episode)	1:37.1	1:44.4	
Median time to first PD peritonitis, days (IQR)	98 (187)	249.5 (260.5)	0.03

ESI = exit-site infection, IQR = interquartile range; PD = peritoneal dialysis.

(43.5%) patients in the non-dressing group (Table 2). The peritonitis rate was 1 per 37.1 patient-months in the dressing group and 1 per 44.4 patient-months in the non-dressing group. Only 1 patient had an inter-relationship organism between peritonitis and previously documented ESI. Adjusting for age, gender diabetes, and duration on PD before recruitment in the study, non-dressing did not significantly increase the rate ratio for ESI (incidence rate ratio [IRR] = 1.94, *p* value = 0.39) or peritonitis (IRR = 0.76, *p* value = 0.46).

There was no gram-positive peritonitis in the non-dressing group in contrast to the dressing group (Table 2). The median time to the first peritonitis episode was significantly shorter in the dressing group (*p* = 0.03).

DISCUSSION

In our study, simple washing and cleansing of the exit site during a normal shower followed by application of antimicrobial

cream alone after drying, without antiseptic or dressing cover, did not increase the incidence of PD infection. In our study population, ESI rates of $\geq 1:200$ episodes per patient-months were very low and the observed peritonitis rate was below the ISPD recommendation of 1 in 18 patient-months (13). The rates of ESI are highly variable within Malaysia and between countries, with reported rates in adults ranging between 0.05 – 1.02 episodes/patient-year (26,27). The non-dressing method used in our study is also advantageous as it avoids exposure to topical skin irritants such as antiseptic liquid and dressing film, reduces unnecessary time spent and cuts the cost of disposables used.

Our study supports a previous 2-year randomized control trial (RCT) of 60 continuous ambulatory PD patients that did not find any significant difference in the rate or risk of infection between groups following different exit-site care protocols (28). In that study, 1 group followed a simple wash and shower technique where a cover dressing was optional ($n = 30$), whereas the other group followed a protocol requiring an occlusive dressing to remain over the exit site during showering and replacement of the dressing afterwards using a dressing pack and an occlusive dressing ($n = 30$).

A smaller RCT also had similar results that showed patients who used a routine cleaning procedure with a dressing over the exit site ($n = 10$) had no significant difference in the number of infections compared to those using the same procedure but who left the exit site open ($n = 3$) (29). In another study, 32 prevalent adult PD patients were randomized to 1 of 3 groups. A conventional dressing of gauze ($n = 11$), transparent OpSite (Smith & Nephew, Dubai, UAE) dressing ($n = 7$), or no dressing ($n = 9$) was used, and patients were followed for assessment of infection for a period of 6 weeks. By intention-to-treat analysis, the OpSite method did not result in different infection rates compared with the other treatments; however, a considerable proportion of patients did not tolerate OpSite as a dressing due to itching (30).

Mupirocin cream has been shown to be very effective in preventing *S. aureus* ESI (20–22), preventing 63% of *S. aureus* PD-related infection, and has been recommended by the ISPD for *S. aureus* prophylaxis. The emergence of organisms with mupirocin resistance and treatment failure with mupirocin (23,24) have been reported and are of significant concern. In contrast to these previous studies, we found no emergence of *S. aureus* resistance to mupirocin in our cohort.

An important finding in our study was the absence of *P. aeruginosa* ESI and no increased risk of developing *S. aureus* ESI in the non-dressing group as compared to the dressing group. This is interesting as we always presumed that meticulous dressing and covering of the exit site with film or gauze dressing is the best way to prevent exit-site contamination. We can hypothesize from this study that the covered dressing itself may actually be the pathway for organisms to contaminate the exit site. A covered dressing does not provide an inhibitory effect on micro-organism growth but, conversely, provides a milieu for accelerated bacterial growth. Our study suggests that this risk can be reduced or prevented by exposing the

exit site and we recommend that this should be practised in PD programs.

To the best of our knowledge, this is the first randomized study available to examine whether simply washing the exit site during a shower, with no cleaning procedure, and leaving the exit site uncovered with only topical antibiotic application provides better protection against PD-related infections than using a dressing. There was no impact of dressing disruptions in the occurrence of major PD catheter-related infections. This is a pilot study and a limitation of our study was the open-label design and small sample size. Blinding was not possible as the participants were aware of being either in the dressing or non-dressing group.

CONCLUSION

Exit-site dressing is widely practiced and has been recommended in guidelines to prevent PD-related infection. Our study showed this practice may be of little benefit in reducing the incidence of ESI or PD-related infection. Use of a non-dressing technique with only prophylactic topical mupirocin cream application is just as effective in preventing PD-related infection. It is more cost-effective, convenient for PD patients, and uses fewer disposables.

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All authors contributed to the study design and data interpretation, and were investigators on the study. Lily Mushahar and Lim Wei Mei also contributed to data collection, and Lily Mushahar conducted the statistical analysis.

DISCLOSURES

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