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NEPHROLOGY – ORIGINAL PAPER

Chlorhexidine for routine PD catheter exit-site care

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Abstract
Purpose Although guidelines suggest the routine use of mupirocin or gentamicin at the exit site of PD catheter, our PD unit has been using chlorhexidine gluconate 0.5 % as exit-site care protocol. The aim of this study was to ascertain whether mupirocin application is superior to the traditionally applied chlorhexidine—regarding prevention of exit-site infections and peritonitis in our unit.
Methods Stable incident and prevalent patients of our unit were randomized to apply mupirocin or chlorhexidine at exit site. The study started on July 1, 2010, and continued till December 2014. End point was the first episode of exit-site infection or peritonitis.
Results Sixty-two patients (mean age 58.5 ± 14.6 years) were randomized. At the end of follow-up, there were 33 patients on mupirocin treatment and 29 on chlorhexidine. The two groups had no differences in age, sex, PD vintage or PD mode. The only difference between the two groups was the percentage of patients with diabetes, 28 % in chlorhexidine group versus 10 % in mupirocin group. Mean time of follow-up was 28.46 ± 16.37 months. Twenty-four episodes of infections (peritonitis and exit site) were recorded. Time to first infection episode was 32 months in mupirocin group (95 % CI 21.4–42.5) versus 29 months (95 % CI 8.6–49.4) in chlorhexidine group. The Kaplan–Meier survival analysis revealed no difference in the infections between the two protocols (log-rank test, $p = 0.477$).
Conclusions Mupirocin is not superior in preventing infections comparing with chlorhexidine in this cohort of patients.

Keywords Mupirocin · Peritonitis · Prophylaxis

Introduction

Guidelines suggest the routine use of mupirocin or gentamicin at the exit site of PD catheter [1], as this procedure has been effective in reducing *Staphylococcus aureus* and/or *Pseudomonas aeruginosa* exit-site infection and peritonitis rates in a number of reports [2, 3].

Our PD unit has been using chlorhexidine gluconate 0.5 % (Hibitane®) as exit-site care protocol since 1995, and peritonitis rates have been low (median 0.14 episodes/patient-years). Chlorhexidine is a cationic polybiguanide active against gram-positive and gram-negative organisms and is usually used as skin disinfectant for central-line catheter exit-site care [4, 5]. Limited data exist about the use of chlorhexidine as PD catheter exit-site standard care [6].

The aim of this study was to ascertain whether mupirocin application is superior to the traditionally applied chlorhexidine—regarding prevention of exit-site infections and peritonitis in our unit.

Methods and patients

Both prevalent and incident stable patients were included. Informed consent was obtained. Exclusion criteria included patients with catheter-related infection or peritonitis at the time of recruitment or in the previous 3 months; use of an oral, intravenous, or intraperitoneal antibiotic at the time

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of randomization or in the past 2 weeks. No patient used nasal mupirocin cream. Routine exit-site care by the patient consisted of application of a small amount of cream around the catheter exit site using a swab or chlorhexidine by a gauze on everyday schedule. All patients were trained by the nurses of the unit. The exit site was examined by the physician and the nurse at each monthly clinic visit. Exit-site infections and peritonitis were defined according to ISPD guidelines. Treatment for infections was according to the unit protocol, and antibiotics were adjusted according to minimum inhibition concentrations (MIC). Patients were randomized to apply mupirocin or chlorhexidine at exit site. The study started on July 1, 2010, and continued till December 2014. End point was the first episode of exit-site infection or peritonitis.

Statistical analysis

Data were expressed as mean values (±SD) or median (range), according to the distribution. Fisher exact test compared group proportions, while continuous variables were compared by the t test. Primary end point was the first episode of exit-site infection or peritonitis. Censoring was defined as transplantation, death or switch to hemodialysis. Time to infection was analyzed using Kaplan–Meier survival analysis and log-rank test.

Results

Sixty-two patients (mean age 58.5 ± 14.6 years) were randomized. At the end of follow-up, there were 33 patients on mupirocin treatment and 29 on chlorhexidine. The two groups had no differences in age, sex, PD duration or PD mode. The only difference between the two groups was the percentage of patients with diabetes, 28 % in chlorhexidine group versus 10 % in mupirocin group (Table 1). Mean time of therapy follow-up was 28.46 ± 16.37 months (median 23.5 months, range 3–53 months). No death or removal of the catheter due to infection was recorded during the study. No side effect related to the use of mupirocin or chlorhexidine was reported.

Twenty-four episodes of infections (peritonitis and exit site) were recorded. The number of events was 13 for mupirocin group (six of them due to staphylococcus species) and 11 in chlorhexidine group (5 due to staphylococcus). The exit-site infection rate was 0.058/patient-years and 0.066/patient-years for gram-positive species in mupirocin and chlorhexidine group, respectively (not statistical significant) (Table 2). Peritonitis rates was 0.034/patient-years and 0.066/patient-years for gram-positive species in mupirocin and chlorhexidine group and 0.046 versus 0.05 for gram negative in the groups, respectively (Table 2).

Table 1 Characteristics of the group

	Mupirocin ($n = 33$)	Chlorhexidine ($n = 29$)	p
Age (years)	57.7 ± 14.8	59.7 ± 15.4	ns
Female (%)	12 (41)	9 (36)	ns
PD duration (months)	3 (0–96)	10 (0–113)	ns
Incident patients (%)	15 (51 %)	13 (52 %)	ns
Automated PD (%)	10 (34.4)	11(44)	ns
Diabetes (%)	3 (10 %)	7 (28 %)	$p = 0.03$
Davies comorbidity index			
Low	57.6 %	55.2 %	ns
High	6 %	10 %	ns
Albumin (g/dl)	3.66 ± 0.36	3.77 ± 0.30	ns

Total duration of the study was 1040 patient-months for the mupirocin group and 725 patient-months for the chlorhexidine group. The infection rate in mupirocin group was 0.15 episodes/patient-years, while in chlorhexidine group was 0.18 episodes/patient-years (p NS).

Time to first infection episode was 32 months in mupirocin group (95 % CI 21.4–42.5) versus 29 months (95 % CI 8.6–49.4) in chlorhexidine group. The Kaplan–Meier analysis revealed no difference in the infection rates between the two protocols (log-rank test, $p = 0.477$) (Fig. 1).

Discussion

Our trial has proved that chlorhexidine is as effective as mupirocin in preventing PD infections (exit site and peritonitis) in our unit. Although time to first episode was longer in mupirocin group, this difference was not statistical significant in analysis, even though chlorhexidine group had more diabetic patients.

The ideal exit-site treatment should include antibiotics against both gram-positive and gram-negative microbes. Prophylaxis using daily application of mupirocin to the skin around the exit site has been effective in reducing *Staphylococcus aureus* exit-site infection and peritonitis rates. However, mupirocin resistance has been reported [7] and Pseudomonas has emerged lately as an important cause of infection [8]. Gentamicin use at exit-site care was proposed instead of mupirocin in a number of trials [9]. However, resistance has been reported [10], and concerns for increase in fungal infections have been aroused [8]. Recently, antibacterial honey was compared with standard protocols in an Australian study, but no superiority results were proven [11].

Our unit has been using chlorhexidine as exit-site care protocol for two decades. The bactericidal effect of

Table 2 Exit-site and peritonitis episodes in both groups

	Mupirocin		Chlorhexidine	
	Number	Rate (infection/patient-years)	Number	Rate (infection/patient-years)
Exit site				
Gram positive	5	0.058	4	0.066
Staphylococcus aureus	3		3	
Streptococcus spp	2		1	
Gram negative	1	0.011	0	0
Klebsiella sp	1			
Escerichia coli	–			
Peritonitis				
Gram positive	3	0.034	4	0.066
Staphylococcus aureus	3		2	
Streptococcus spp			1	
Coagulase-negative staphylococcus			1	
Gram negative	4	0.046	3	0.05
Enterobacter clocae			1	
Escerichia coli	3		2	
Klebsiella sp	1		–	

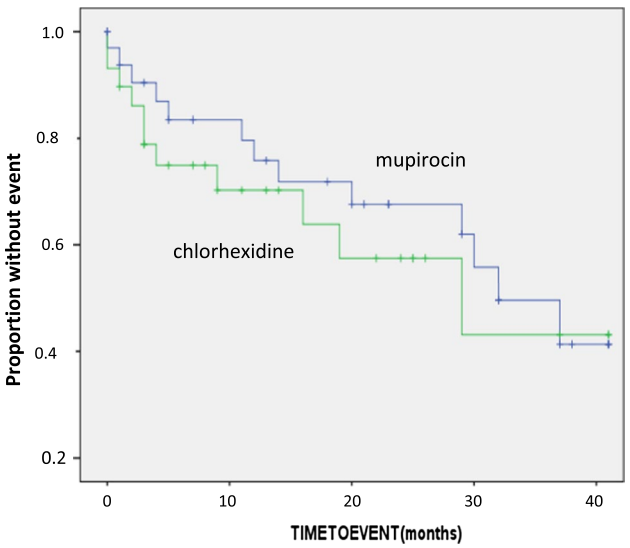

Fig. 1 Kaplan–Meier lines showing time to first infection in patients on mupirocin versus chlorhexidine applied to the exit site

chlorhexidine is a result of the binding of this cationic molecule to negatively charged bacterial cell walls. In the literature, the majority of data concern its use as local skin antiseptic. Regarding hemodialysis catheter exit-site care, a number of studies have investigated its efficacy comparing it with povidone or alcohol-based solutions with mostly positive results [5, 12, 13]. Its use as PD catheter exit-site care has been tested (vs povidone) in only one study [6], which concluded that these agents had no differences in preventing infections. To our knowledge, no study has compared chlorhexidine to mupirocin so far.

Our trial is an open-label one, and the small number of events limits the statistical analysis. However, it implies obviously that each unit can use its own preventive protocols as far as they are successful in reducing infection rates.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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