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Microbial pattern of peritoneal catheter infection: is there a non-diphteria corynebacteria emergence?

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SUMMARY

Background: *A prospective cohort study was undertaken to compare the rates of the infecting microorganisms of the peritoneal catheter exit-site in three periods of the prophylactic protocol of a peritoneal dialysis program. All patients treated for more than one month on Peritoneal Dialysis were included: Fourty-eight in Period 1 (P1), 48 in Period 2 (P2), and 54 in Period 3 (P3). Each period was of 3 years.*

Methods: *Infection prophylaxis protocol: P1: hydrogen peroxide or povidone iodine and non-occlusive dressing; P2: sterile water (boiled water) instead of antiseptic agents, semi-permeable dressing for taking showers, and nasal mupirocine prophylaxis for Staphylococcus aureus carriers; P3: equal to P2, plus local application of antibiotics in equivocal exit-site for infection and argentic nitrate in granulation tissue. Main outcome measure: the rates of catheter infection and microorganisms causing infection were analysed by means of the Poisson regression method. Chi-square and ANOVA when appropiate.*

Results: *The proportion of catheters implanted by nephrologist or surgeon ($p < 0.01$) and modality treatment by CAPD or CCPD ($p < 0.0001$) were significantly different in the three periods, while the Staph. Aureus carrieres was in the limit of significance ($p = 0.048$). Throughout the three periods, a significantly decreasing rate of total ($P = 0.0035$) and acute infections ($P < 0.001$), Staph. aureus ($P = 0.003$) and peritonitis ($P = 0.0025$) were found. The Pseudomonas aer. ($P = 0.006$) and Gram negative Bacteria ($P = 0.023$) decreased significantly in P2. The multiple factor analysis included eight factors: sex, age group, ESRD, DM, catheter implatation (nephrologist, surgeon), modality treatment (CAPD, CCPD), manufacturer and prophylaxis period as possible predictors of the catheter infections, the specific microorganisms and the peritonitis. That analysis revealed the prophylaxis period as the main predictive factor of the improvements found ($p < 0.02$,- $p < 0.001$). In contrast, the Corynebacteria spp increased significantly ($P=0.008$) throughout the three periods. One half of the Corynebacteria in each period could be considered colonisers. The other half caused true infections, but not one of those episodes required catheter intervention. The non-diphtheria Corynebacteria increase was found related with the continuous cycling Peritoneal Dialysis treatment in multiple factor analysis ($p = 0.0023$) and in the proportion analysis ($P = 0.039$, χ^2).*

Conclusion: *The progressive protocol applied obtained good results, without the continued use of local antiseptics or antibiotics at the exit-site. However, the non-*

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diphtheria Corynebacteria sp infection increment favours the consideration of an antiseptic agent for the exit-site care.

Key words: ***Peritoneal dialysis catheter infection. Prophylaxis. Microorganisms. Corynebacterium.***

PATRÓN MICROBIOLÓGICO DE LA INFECCIÓN DEL CATÉTER PERITONEAL: ¿AUMENTO DE CORYNEBACTERIUM SP?

RESUMEN

En un estudio de cohorte se observaron prospectivamente los gérmenes causantes de infección en el catéter peritoneal en tres protocolos de profilaxis consecutivos, de 3 años cada uno. Pacientes con más de un mes de permenencia en Diálisis Peritoneal: 48 en el período 1 (P1), 48 en el período 2 (P2) y 54 en el período 3 (P3).

Métodos: *La profilaxis de infección del catéter fue: P1: Peróxido de hidrógeno o Povidona yodada y apósito no oclusivo; P2: Agua estéril (hervida), apósito semipermeable para la ducha y mupirocina nasal para los portadores de Staf. aureus; P3: igual que en el período anterior añadiendo antibióticos locales para los orificios equivocos de infección y aplicación de nitrato de plata en el tejido de granulación. Análisis estadístico: regresión de Poisson, χ^2 y ANOVA.*

Resultados: *A través de los 3 períodos hubo una disminución significativa de la tasa de infecciones totales (aguda, crónica y del manguito) (p = 0,0035), agudas (p < 0,001), las causadas por Staph. aureus (p = 0,003) y también de las peritonitis (p = 0,0025). Las infecciones por Pseudomonas aer. (p = 0,006) y por gérmenes gram negativos (p = 0,023) disinuyeron significativamente en el P2. El análisis multifactorial confirmó el período de profilaxis como el principal factor predictivo de los cambios en las tasas de infección y de los microorganismos específicos (p entre < 0,02 y < 0,001). Sin embargo las infecciones por Corynebacterium sp aumentaron significativamente (p = 0,008) a través de los tres períodos. En el análisis de factores este aumento de infecciones por Corynebacterium sp se halló relacionado con el tratamiento con Diálisis Peritoneal continua cíclica (DPCC) en el análisis multifactorial (p = 0,0023) y en el de proporciones (p = 0,039).*

Conclusión: *El protocolo de profilaxis de la infección del orificio del catéter de DP aplicado, sin usar continuadamente antisépticos o antibióticos locales, ha demostrado buenos resultados para la mayoría de microorganismos. Sin embargo el aumento de infecciones por Corynebacterium sp obliga a considerar la aplicación de antisépticos locales.*

Palabras clave: ***Infección del catéter peritoneal. Profilaxis. Diálisis peritoneal. Microorganismos. Corynebacterium.***

INTRODUCTION

Peritoneal catheter infections lead to prolonged antibiotic therapy, cause 10%-25% of peritonitis cases, account for 8%-39% of catheter replacements or elimination, and my be the cause peritoneal dialysis withdrawal in 2%-37% of the cases.[1]

Catheter care for infection prevention varies from daily cleansing with soap or antiseptic soap, to the use of different antiseptic solutions or topical application of antibiotics.[2-6]

Specific prophylaxis in nasal carriers of *Staphylococcus aureus* has dramatically decreased *Staph. aureus*-induced catheter and peritoneal infections[7-10] but not catheter infections due to gram-negative microorganisms.[11]

Other prophylactic regimens focused on specific microorganisms such as *Pseudomonas aeruginosa*

and gram-negative bacteria (GNB) have not been tried until recent works[12-13] in which continuous antibiotic therapy has been applied into the catheter outlet of treated patients.

However, long-term use of antibiotics may induce the emergence of resistant microorganisms, as it has occurred with mupirocin.[14,15,16]

Thus, although important advances have been achieved regarding prevention of peritoneal catheter infections and peritonitis, the optimal prophylaxis prevention in chronic catheter care is yet to be determined.[6,17]

We have retrospectively studied the diagnoses of peritoneal catheter outlet and the microbiological pattern in catheter infections in a cohort of peritoneal dialysis (PD) patients submitted to a stepwise infection prophylaxis protocol; we thereby present the outcomes.

METHODS

A cohort study has been carried out in all patients with more than one month in PD therapy in order to assess the diagnoses of the catheter outlet, the incidence of catheter infection, and infecting microorganisms, by applying three successive infection prophylaxis protocols, each one of them lasting for three years, since 1993.

Diagnostic method of the catheter outlet

The Twardowski and Prowant method[18] assessing the status of the catheter outlet was adapted with a photographic diagnostic technique[19] that was used for this study. In brief, the signs and symptoms of the outlet neighborhoods were scored 0-6 according to the following diagnosis: 0 = Perfect (P), 1 = good status (G), 2 = Doubtful (D), 3 = acute infection (A), 4 = Chronic infection (C), 5 = Cuff infection (C), and 6 = traumatic (T).[18]

Assessment of catheter outlet

Bimonthly the catheter outlet was assessed (with magnification lens as required) recording the scored for each attribute and with the summary diagnosis at each evaluation. The diagnosis was made by a single observer (JT) that performed or supervised all evaluations throughout the study.

At each assessment and when infection was suspected, a swab from the catheter outlet was taken and carried in Stuart's media for later microbiological culture in standard media in order to identify colonizing or infecting organisms.

A sample from the nostrils was taken to detect the presence of *Staph. aureus*. The carrier status was defined in those patients with positive nasal or catheter culture for *Staph. aureus* at any time of the study.

Catheter infection prophylaxis protocol

Period 1: daily showering with antiseptic soap, application of hydrogen peroxide or povidone iodine as disinfectants, and non-occlusive dressing (gauze); oral nistatin as fungal prophylaxis in prolonged antibiotic therapies.

Periods 2 and 3: cleansing of the catheter outlet with sterile (boiled) water without disinfectants, mandatory semi-permeable dressing (Tegaderm or Opsite flexigrid) when showering in order to avoid outlet contamination with tap water; the bath was not allowed; nasal mupirocin 5 days per month as prophylaxis in *Staph. aureus* carriers; fluconazol as fungal prophylaxis.

Period 3: the same as P2, adding cauterization of the granulation tissue with silver nitrate and local application of antibiotics at doubtful catheter outlets for any organism.

Catheter infections and peritonitis were treated with oral or parenteral antibiotics according to usual regimens. For infection recurrences due to the same organism, a second antibiotic course was given, after which the catheter cuff was excised or the catheter replaced. In peritonitis due to the same microorganism found at the catheter outlet the catheter was replaced. Special attention was placed on catheter care and hygiene procedures during patients' training and follow-up in order to comply with the study protocol and no other changes were introduced but those mentioned above.

PATIENTS

All patients with more than one month in the Peritoneal Dialysis program have been included for 9 years. Patients may have participated in tow consecutive periods, the corresponding time at risk being calculated for each period. Treatment modalities were: Continuous ambulatory peritoneal dialysis (CAPD) with 3-5 replacements of 2 L/day, and Cycled Continuous Peritoneal Dialysis (CCPD) with 12-20 L/day distributed in 6-9 nocturnal cycles and 1-3 diurnal cycles.

The study protocol was approved by the Ethics and Clinical Research Committee from the participating

Table I. Patient characteristics by prophylaxis periods

Period	1: n (%)	2: n (%)	3: n (%)	χ^{2}[1]
Patients	48	48	54	
Age: mean (SD)	57.75 (15,24)	55.94 (16,21)	53.22 (15,24)	NS[2]
Gender: male	29 (60%)	31 (65%)	39 (72%)	NS
Diabetes mellitus	13 (27%)	19 (40%)	22 (41%)	NS
Nephrologist-inserted catheter	20 (42%)	34 (71%)	25 (46%)	P < 0.01
Surgeon-inserted catheter	28 (58%)	14 (29%)	29 (54%)	
Treatment modality				
CAPD	37 (77%)	29 (60%)	15 (28%)	P < 0.0001
CCPD	11 (23%)	19 (40%)	39 (72%)	
S. aureus carriers	17 (35%)	26 (54%)	17 (31%)	P = 0.048
Observation period: months	702	682	794	

Note:
[1] χ^{2}: chi-squared, 2 x 3 table.
[2] One-factor ANOVA.

hospitals and patients accepted their participation into the study.

STATISTICS

Comparison of continuous variables was done by ANOVA test and the qui-squared test was used for discrete variables. Comparison of infection rates (episodes /patient-year) and factor analysis was done by the Poisson's regression model using the Newton Raphson's algorithm and backwards elimination (Egret for Windows, 2003; CYTEL software corporation Cambridge, MA, USA).

RESULTS

The characteristics of the patients included at the different periods are shown in Table I. There were no differences by age, gender, primary renal disease (PRD), or diabetes mellitus (DM). The ratio of catheters placed by the surgeon or by the nephrologist ($p < 0.01$, c^{2}) and treatment modality ($p < 0.0001$) were significantly different for the three study periods, whereas the ratio of *Staph. aureus* carriers was close to be significant ($p = 0.048$).

Diagnoses of the catheter outlet labeled as Perfect or Good Status had a significant increase were as acute and total infections and peritonitis significantly decreased in the three study periods (Table II and Fig. 1). Doubtful evaluations slightly decreased at P3. Chronic infections and cuff infections did not significantly varied.

The analysis of microorganisms causing infection showed a significant decrease of *Staph. aureus* (Table III). *Pseudomonas aeruginosa* and other gram-negative organisms significantly decreased at P2, but increased again at P3. Five out of 8 episodes of *Pseudomonas aeruginosa infection* at P3 were related to patient taking a shower without adequate catheter outlet protection or not having done appropriate care after the shower.

Corynebacterium sp. infections significantly increased throughout the three study periods. These episodes were due to *Corynebacterium* as the single microorganism in 2/6 at P1, 9/17 at P2, and 11/21 at P3. In the remaining episodes, *Corynebacterium* was isolated together with other organisms, mainly staphylococci, so that *Corynebacterium* may be considered as a colonizing agent. None of the infections caused by *Corynebacterium* led to any kind of intervention on the catheter.

Eight controlled factors were introduced into the regression model as likely predictors of catheter infection, peritonitis, and of the kind of organism infecting the catheter: gender, age, PRD, DM, technique of catheter placement (manual/surgical), moda-

Table II. Diagnóses from assessment of the catheter outlet and peritonitis episodes (Rates per patient-year)

Period	1: pe/p-y	2: pe/p-y	3: pe/p-y	Poisson's regression P1 # P2	P1 # P3
Risk time (Patients-year)	(60.58)	(59.00)	(62.25)		
Perfect and good status	2.71	3.4	3.74	0.029	0.0014
Equivocal	1.80	1.90	1.35	0.69	0.048
Acute infection	0.86	0.30	0.26	< 0.001	< 0.001
Chronic infection	0.10	0.07	0.14	0.56	0.47
Cuff infection	0.46	0.32	0.45	0.22	0.92
Total infections catheter	1.42	0.69	0.85	< 0.001	0.0035
Peritonitis	1.11	0.93	0.59	0.35	0.0025

Note: Comparison by Poisson's regression model: P1 # P2: Period 1 compared with period 2; P1 # P3: Period 1 compared with period 3.

lity (CAPD/CCPD), manufacturer, and prophylaxis period (Table IV). The prophylaxis period was the main predictive factor for total catheter infections, acute infections, and infections with *Staph. aureus, Pseudomonas aeruginosa*, and other gram-negative organisms infections. By contrast, treatment modality was significant for *Corynebacterium sp*. infections ($p = 0.0023$). The ratio of patients infected with *Corynebacterium sp*. was calculated finding that it was greater with CCPD (cycled) than with CAPD ($p = 0.039$, c^2).

The course of conventionally antibiotic treated-catheter infections was complete resolution in 92.8% of the cases. Catheter interventions due to persistent infections, recurrences, or peritonitis were 12 at P1, 13 at P2, and 5 at P3 ($p = 0.09$). Seventeen catheter withdrawals were due to peritonitis, eight to simultaneous catheter infection and peritonitis, and 5 to isolated catheter infection. The rates of infection-induced catheter loss were: 0.08 p/y at P1, 0.17 p/y at P2, and 0.06 p/y at P3, with no significant differences between the three periods.

DISCUSSION

The prophylaxis of peritoneal catheter infection by means of a progressive protocol implemented during three different periods in this prospective cohort observational study achieved decreasing the number of acute and total infections, as well as peritonitis and *Staph. aureus* microorganisms throughout the three study periods, and of *Pseudomonas aeruginosa* and GNB at P2.

The multifactorial analysis confirmed that the prophylactic period was the most significant factor for outcomes improvement. We cannot rule out personnel experience and other factors difficult to control, which may have improved with time, as other factors influencing the results. Special care was put on preventing deviations in protocol implementation during this study. Thus, outcomes improvement should be mainly attributed to prophylaxis applied during the different study periods.

Study limitations

We may raise the following limitations: 1) infection rate of the catheter outlet is higher than that currently described in the literature, and 2) the rate of negative cultures (11%-19%) is high. Actually, the method for classifying and diagnosing the status of the catheter outlet implies certain degree of systematic infection over-diagnosis because it is based on inflammatory signs, granulation, lack of epithelium, etc., that in some cases may not have reached the level of overt infection with the classical purulent discharge. Besides, the lack of pus may lead to negative culture in phases that other authors would classify as pre-infection. This is a matter of debate since there is no unanimous agreement among the experts or international guidelines.[6] In this work a highly systematic and detailed assessment method of the catheter outlet has been applied allowing for an accurate follow-up of the course of the outlet making possible the comparison between the different study periods.

Table III. Microorganisms isolated at catheter infection episodes by study period

Period	1: n (%)	2: n (%)	3: n (%)	χ^2[1]
Total Infection Episodes	86	41	53	
Positive culture	70 (81)	33 (81)	47 (89)	NS
Positive culture with 2 microorganisms	14 (18)	12 (24)	15 (29)	NS
	n (rate)	**n (rate)**	**n (rate)**	**Poisson's regression[2] P1 # P2** / **P1 # P3**
Microorganisms Total	84	45	62	
Staph. C N/ep	21 (0.35)	12 (0.20)	15 (0.24)	ns / ns[3]
Staph. aureus	20 (0.33)	9 (0.15)	4 (0.06)	0.054 / 0.003
Corynebacterium	6 (0.10)	17 (0.29)	21 (0.34)	0.025 / 0.008
Pseudomonas aer	17 (0.28)	1 (0.02)	8 (0.13)	0.006 / 0.069
Candida sp	2 (0.03)	0 (0.0)	3 (0.05)	– / –[4]
Echerichia coli	4	2	2	
Enterobacter	2	0	3	
Serratia	3	1	1	
Proteus mirabilis	2	1	2	
(Total gram-negatives)	(11) (0.30)	(4) (0.10)	(8) (0.18)	0.023 / ns[3]
Others	7	2	3	– / –[4]

Notes:
[1] χ^2: chi-squared, 2 x 3 table.
[2] Poisson's regression model: comparisons between periods P1 # P2 and P1 # P3.
[3] Ns: p > = 0.10.
[4] –: not sufficient data to reach convergence.
[5] (rate): episodes/patients-year.

When reviewing prevention/infection of the peritoneal catheter we will focus our discussion on three issues: Staphylococcus aureus, GNB (*Pseudomonas*), and *Corynebacterium*.

Staphylococcus aureus: In the literature, prophylaxis in *Staph. aureus* carriers with mupirocin has decreased the rate of catheter infections[7,8,9,17,20] and peritonitis,[8,9] but not those by GNB,[8,9,11] except in one study.[21]

The emergence of mupirocin-resistant bugs[14,15,16] and the increase of GNB infections[8] and colonizations[22] has raised concern on its long-term application. The inclusion of mupirocin prophylaxis in our protocol has achieved low catheter infection rates (P3: 0.06 pe/p-y), which is in agreement with other authors (0.22-0.02 pe/p-y),[7,8,12,13,17] although we have not detected resistances to mupirocin throughout the study.

GNB and *Pseudomonas:* Routine prophylaxis for GNB including *Pseudomonas aeruginosa* has not previously been tried until recently in works using ciprofloxacin[12] or gentamycin[13] in all treated patients. In these works, no resistant microorganisms were reported after a mean follow-up period of 22.6 and 23.1 months in the study with ciprofloxacin [12] and after 9.78 and 11.52 months in the study with mupirocin vs. gentamycin.[13] This follow-up times may be relatively short in order to rule out long-term occurrence of resistances. In our protocol we have followed the strategy of avoiding contact of the catheter outlet with tap water by using a semi-permeable dressing (barrier effect) during the shower.[23] In the literature it has

Table IV. Multifactorial analysis of variables predicting catheter infections, specific microorganisms, and peritonitis Poisson's regression model with Newton Raphson algorithm)

Target variable	Predictive variables acceptes by the model	Variables sign.	P	RR	95% confidence interval (min.	max.)
Total catheter infections	Gender + PRD + Modality + Period	Period 2:	< 0.001	0.50	(0.33)	(0.75)
		Period 3:	0.0063	0.57	(0.38)	(0.85)
		Modality CCPD:	0.019	1.50	(1.07)	(2.10)
		PRD DM:	0.015	1.46	(1.08)	(1.98)
Acute infection	Gender+ Period	Period 2:	< 0.001	0.39	(0.24)	(0.62)
		Period 3:	< 0.001	0.29	(0.18)	(0.49)
Cuff infection	Gender + DM + Modality + Period	Female gender:	0.0023	2.13	(1.31)	(3.46)
		DM:	0.03	1.72	(1.05)	(2.81)
		Modality CCPD:	< 0.001	2.46	(1.47)	(4.12)
		Period 2:	0.026	0.48	(0.26)	(0.92)
Staph. ep. / CN	Gender + DM + Modality + Period	Female gender:	0.026	1.99	(1.09)	(3.66)
		Modality CCPD:	0.032	1.99	(1.06)	(3.75)
		Period 2:	0.052 (ns)	0.47	(0.22)	(1.01)
		Period 3:	0.049	0.48	(0.23)	(0.99)
Staph. aur.	Génder + PRD + Implant. + Period	ERP Diversos:	0.012	4.0	(1.35)	(11.84)
		Manual placement:	0.012	2.98	(1.27)	(7.01)
		Period 2:	0.0065	0.31	(0.13)	(0.72)
Corynebacterium	Placement + Modality	Madality CCPD:	0.0023	2.72	(1.43)	(5.19)
Pseudomonas aer.	Manufacturer + Period	Period 2:	0.0063	0.06	(0.008)	(0.45)
Others gram-negatives	Modality + Period	Madality CCPD:	0.02	2.34	(1.14)	(4.81)
		Period 2:	0.015	0.31	(0.12)	(0.79)
		Period 3:	0.033	0.41	(0.18)	(0.93)
Peritonitis	PRD + Implant. + Modality + Manufacturer	Manual placement:	0.02	0.65	(0.45)	(0.93)
		Modality CCPD:	0.007	0.56	(0.37)	(0.86)
		Manufacturer 2:	< 0.001	2.22	(1.60)	(3.06)

Notes:
[1] All predictive variables were introduced for each target variable: gender, age group, PRD, DM, Placement (manual, surgical), Modality (CAPD, CCPD), Manufacturer, Period (P1, P2, P3), backwards elimitation was applied. NS = not significant ($p > 0.05$).

been seldom proposed avoiding contact of the catheter outlet with no sterile water.[24] Our data point out the importance of this mechanism when *Pseudomonas* microorganisms are present in tap water. Moreover, we have verified that in most of the cases the occurrence of *Pseudomonas* is related with the lack of adherence to the protocol instructions.

Corynebacterium spp: There was a significant and unexpected increase of *Corynebacterium sp*. infections during the second and third stages of this study. Coryneform bacteria different from *C. Diphtheriae* have generally been considered as colonizing or contaminating agents, although they may cause severe nosocomial infections in immunosuppressed patients[25] or carrying a catheter.[26,27]

In peritoneal dialysis, *Corynebacterium sp*. or diphtheroid bacteria[28-30] that may have been categorized as «other gram-positives»[31] have caused 4%-7% of peritoneal infections. It is interesting to know that *Corynebacterium* subspecies have been mainly described in PD as peritonitis «cases»[30,32-34] and less frequently as catheter infections.[27,30,31] More recently, Schiffl and others[35] have described a series of 8 cases with 12 episodes of non-diphtheroid *Corynebacteria*, accounting for 9% of all infections of the peritoneal catheter outlet in one center, raising the question of whether or not they should be considered as emergent nosocomial pathogens in CAPD.

We have not available subspecies identification in our series in order to assess their different pathogenicity. In fact, only half of isolated *Corynebacteria* at

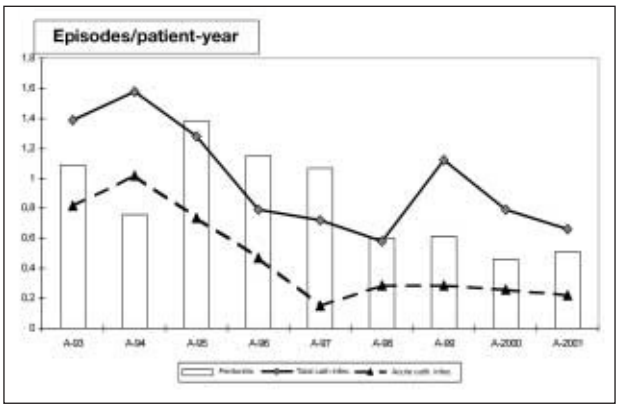

Fig. 1.—Annual rates of total catheter infections (diamonds), acute infections (triangles) and peritonitis (bars).

each one of the stages may be considered as true infecting agents since the other half were accompanied by other microorganisms that could have been the ones causing the infection.

The analysis by treatment subgroups and the multifactorial analysis found a relationship between these infections and CCPD therapy. It is difficult to define the reason for the increase in *Corynebacteria* infections in our protocol. The different hypotheses are: a) the lack of an antiseptic solution in the care of the catheter outlet allowing in this way the increase of skin colonizing agents; b) the semipermeable dressing might have favored moist at the catheter outlet; c) some maneuver related with connecting the catheter to the cycling device or with tractions during the therapy. However, hypotheses a) and b) would not explain the increase in the cycling device. In fact, we cannot assure the reason but we consider Corynebacterium-related catheter infections important enough to consider the inclusion of some antiseptic remedy in the protocol of catheter care.

In summary, in this progressive protocol of prophylaxis of peritoneal catheter infection we have avoided continuous use of antiseptic or local antibiotics, achieving a decrease in acute infections, total infections, and infections due to *Staphylococcus aureus* and partially *Pseudomonas* and GNB at P2. However, *Corynebacterium* infections significantly increased and were related to the use of a cycling device. This increase of *Corynebacteria* raises the issue of whether applying or not an antiseptic at the catheter outlet.

REFERENCES

1. Gupta B, Bernardini J, Piraino B: Peritonitis associated with exit-site and tunnel infections. *Am J Kidney Dis* 28: 415-9, 1996.
2. Luzar MA, Brown CB, Balf D, Hill L, Issad B, Monnier B y cols.: Exit-site care and exit-site infection in CAPD: results of a randomized multicenter trial. *Perit Dial Int* 10: 25-9, 1990.
3. Prowant BF, Warady BA, Nolph KD: Peritoneal dialysis catheter exit-site care: results of an international survey. *Perit Dial Int* 13: 149-54, 1993.
4. Piraino B: Exit-site care. *Perit Dial Int* 16 (Supl. 1): S336-9, 1996.
5. Lewis SL, Prowant BF, Douglas C, Cooper CL: Nursing practice related to peritoneal catheter exit-site care and infections. *ANNA J* 23: 609-15, 1996.
6. Piraino B, Bailie GR, Bernardini J, Boeschoten E, Gupta A, Holmes C, Kuijper Ed J, Kam-Tao Li Ph y cols.: (ISPD *Ad hoc* advisory committee on PD related infections). Peritoneal Dialysis-related infections recommendations: 2005 update. *Perit Dial Int* 25: 107-131, 2005.
7. Zimmerman SW, O'Brien M, Wiedenhoeft FA, Johnson CA: *Staphylococcus aureus* peritoneal catheter-related infections: a cause of catheter loss and peritonitis. *Perit Dial Int* 8: 191-4, 1988.
8. Pérez-Fontán M, García-Falcón T, Rosales M, Rodríguez-Carmona A, Adeva M, Rodríguez-Lozano I y cols.: Treatment of *Staphylococcus aureus* nasal carriers in CAPD with mupirocin: long-term results. *Am J Kidney Dis* 22: 708-12, 1993.
9. Bernardini J, Piraino B, Holley J, Johnston JR, Lutes R: A randomized trial of *Staphylococcus aureus* prophylaxis in peritoneal dialysis patients: mupirocin calcium ointment 2% applied to the exit-site *versus* cyclic oral rifampin. *Am J Kidney Dis* 27: 695-700, 1996.
10. Ritzau J, Hoffman RM, Tzamaloukas AH: Effect of preventing *Staphylococcus aureus* carriage on rates of peritoneal catheter-related staphylococcal infections. Literature synthesis. *Perit Dial Int* 21: 526-7, 2001.
11. Piraino B, Bernardini J, Florio R, Fried L: *Staphylococcus aureus* prophylaxis and trends in gram-negative infections in peritoneal dialysis patients. *Perit Dial Int* 23: 456-9, 2003.
12. Montenegro J, Saracho R, Aguirre R, Martínez I, Iríbar I, Ocharán J: Exit-site care with ciprofloxacin otologic solution prevents polyurethane catheter infection in peritoneal dialysis patients. *Perit Dial Int* 20: 209-14, 2000.
13. Bernardini J, Bender F, Florio T, Slonad J, Palmmontalbano L, Fried L, Piraino B: Randomized, double-blind trial of antibiotic exit-site cream for prevention of exit-site infection in peritoneal dialysis patients. *J Am Soc Nephrol* 16: 539-45, 2005.
14. Pérez-Fontán M, Rosales M, Rodríguez-Carmona A, Falcón TG, Valdés F: Mupirocin resistance after long-term use for *Staphylococcus aureus* colonisation in patients undergoing chronic peritoneal dialysis. *Am J Kidney Dis* 39: 337-41, 2002.
15. Annigeri R, Conly J, Vas S, Dedier H, Prakashan KP, Bargman JM y cols.: Emergence of mupirocin-resistant *Staphylococcus aureus* in chronic peritoneal dialysis patients using mupirocin prophylaxis to prevent exit-site infection. *Perit Dial Int* 21: 554-9, 2001.
16. Lobbedez Th, Gardam M, Dedier H, Burdzy D, Chu M, Izatt Sh y cols.: Routine use of mupirocin at the peritoneal catheter exit-site and mupirocin resistance: still low after 7 years. *Nephrol Dial Transplant* 19: 3140-43, 2004.
17. Strippoli GF, Tong A, Johnson D, Schena FP, Craig JC: Antimicrobial agents to prevent peritonitis in peritoneal dialysis: a systematic review of randomised controlled trials. *Am J Kidney Dis* 44: 591-603, 2004.
18. Twardowski ZJ, Prowant BF: Classification of normal and diseased exit-sites. *Perit Dial Int* 16 (Supl. 3): S32-S50, 1996.
19. Teixidó J, Arias N: Catheter exit-site: photographic diagnostic table based on graded attributes (criteria). *Perit Dial Int* 18 (Supl. 1): S40, 1998 (Abstract).
20. Cancho B, Garduño E, Domínguez C, Blanco J, Caravaca F: Resultados a largo plazo de un régimen de descolonización de

Staphylococcus aureus en pacientes en diálisis peritoneal. *Nefrología* 21: 464-70, 2001.
21. Thiam-Seong Lim Ch, Wong K-S, Wai-Yin Foo M: The impact of topical mupirocin on peritoneal dialysis infection rates in Singapore General Hospital. *Nephrol Dial Transplant* 20: 1702-6, 2005.
22. Pérez-Fontán M, Rodríguez-Carmona A, Rosales M, García-Falcón T, Valdés F: Incidence and clinical significance of nasal and pericatheter colonisation by Gram-negative bacteria among patients undergoing chronic peritoneal dialysis. *Nephrol Dial Transplant* 17: 118-22, 2002.
23. Morey A, Lima C, Munar MA, Martínez JG: Estrategias de prevención de la infección del orificio de salida del catéter peritoneal. *Nefrología* 20: 295-6, 2000.
24. Dryden MS, Ludlam HA, Wing AJ, Phillips I: Active intervention dramatically reduces CAPD-associated infection. *Adv Perit Dial* 7: 125-128, 1991.
25. Riebel W, Frantz N, Adelstein D, Spagnuolo PJ: Corynebacterium JK: a cause of nosocomial device-related infection. R*ev Infect Dis* 8: 42-9, 1986.
26. De Witt D, Mulla R, Burns A, Phelps RG: Tenchkoff catheter associated peritonitis caused by *Corynebacterium group* I2. *J Infection* 26: 341-3, 1993.
27. Crabtree JH, García NA: *Corynebacteriun striatum* peritoneal dialysis catheter exit-site infection. *Clin Nephrol* 60: 270-4, 2003.
28. Abraham G, Savin E, Ayiomamitis A, Izatt S, Vas SI, Mathews RE y cols.: Natural history of exit-site infection in patients on CAPD. *Perit Dial Int* 8: 211-6, 1988.
29. De Witt D, Mulla R, Burns A, Phelps RG: Tenchkoff catheter associated peritonitis caused by *Corynebacterium group* I2. *J Infection* 26: 341-3, 1993.
30. Esteban J, Calvo R, Gutiérrez F, Soriano F, Ortiz A, Reyero-López A: Peritonitis due to CDC coryneform group A-4 in a patient undergoing continuous cycling peritoneal dialysis. *Eur J Clin Microbiol Infect Dis* 17: 213-4, 1998.
31. Bernardini J, Holley JL, Johnston JR, Perlmutter JA, Piraino B: An analysis of ten-year trends in infections in adults on CAPD. *Clin Nephrol* 36: 29-34, 1991.
32. Morris AJ, Henderson GK, Bremner DA, Collins JF: Relapsing peritonitis in a patient undergoing CAPD due to *Corynebacterium aquaticum. J Infection* 13: 151-6, 1986.
33. Fernández Girón F, Saavedra Martín JM, Benítez Sánchez M, Fernández Mora F, Rodríguez Gómez E: *Corynebacterium minutissimum* peritonitis in a CAPD patient. *Perit Dial Int* 18: 345-6, 1998.
34. Bhandari S, Meigh JA, Sellars L: CAPD peritonitis due to *Corynebacterium striatum. Perit Dial Int* 15: 88-9, 1995.
35. Schiffl H, Mücke C, Lang SM: Exit-site infections by non-diphteria corynebacteria in CAPD. *Perit Dial Intern* 24: 454-459, 2004.