Revista Argentina de Microbiología
ISSN: 0325-7541
ram@aam.org.ar
Asociación Argentina de Microbiología
Argentina

SANTOIANNI, J. E.; PREDARI, S. C.; VERÓN, D.; ZUCCHINI, A.; DE PAULIS, A. N.
A 15 year-review of peritoneal dialysis-related peritonitis: Microbiological trends and patterns of infection in a teaching hospital in Argentina
Revista Argentina de Microbiología, vol. 40, núm. 1, 2008, pp. 17-23
Asociación Argentina de Microbiología
Buenos Aires, Argentina

ISSN 0325-7541
ARTÍCULO ORIGINAL Revista Argentina de Microbiología (2008) 40: 17-23

A 15 year-review of peritoneal dialysis-related peritonitis: Microbiological trends and patterns of infection in a teaching hospital in Argentina

J. E. SANTOIANNI[1]*, S. C. PREDARI[1], D. VERÓN[2], A. ZUCCHINI[2], A. N. DE PAULIS[1]

[1]Department of Microbiology and [2]Department of Nephrology, Instituto de Investigaciones Médicas Alfredo Lanari, Universidad de Buenos Aires. Avda. Combatientes de Malvinas 3150 (C1427ARO) Ciudad Autónoma de Buenos Aires, Argentina.
**Correspondence. E-mail: josan@fibertel.com.ar*

ABSTRACT

This study reports the infectious peritonitis rates in 44 patients on peritoneal dialysis in three different systems over the last 15 years, covering clinical outcomes, exit-site infections, tunnel infections, causative microorganisms, and the history of susceptibility of organisms causing peritonitis, in order to establish our center-specific selection of empiric therapy. Two microbiological procedures were herein used: method A, where 100 ml of dialysate were centrifuged and cultured in standard media and into blood-culture bottles; and method B, where 10 ml were directly injected into blood-culture bottles. Swabs from the exit-site or tunnel were taken when purulent drainage was observed. There were 96 episodes of peritonitis during 110.43 patient-years (0.87 episodes/patient-year). Sensitivity of method A was 96.88% (93/96 episodes) *versus* 81.25% (78/96) of method B (p= 0.001). Gram stain sensitivity was 36.46%. The etiologic agents were 64 (56.64%) gram-positive cocci, 22 (19.47%) gram-negative fermentative rods, 20 (17.7%) gram-negative non fermentative rods, 5 (4.43%) yeasts, 1 (0.88%) micelial fungus, and 1 (0.88%) anaerobic rod. Fifty-five exit-site infections were documented (0.5 episodes/patient-year). Ceftazidime and imipenem showed excellent activity on gram-negative rods. There were 92.3% of methicillin-susceptible *Staphylococcus aureus* but only 33.3% of methicillin-susceptible coagulase-negative staphylococci; vancomycin was active against 100% of the gram-positive cocci. The clinical outcomes of peritonitis were 73 initial cure, 19 catheter removal and four related deaths. The empiric therapy in our center should be vancomycin plus ceftazidime or imipenem. Once the etiological agent and its susceptibility pattern are known, the de-escalating therapy must be applied to avoid the emergence and spread of vancomycin-resistant microorganisms.

Key words: peritoneal dialysis-related peritonitis, infectious peritonitis rates, exit-site infection, tunnel infection

RESUMEN

Peritonitis en diálisis peritoneal: características microbiológicas y patrones de infección a lo largo de 15 años en un hospital universitario en Argentina. Se comunican las tasas de peritonitis infecciosa de 44 pacientes en tres sistemas diferentes de diálisis peritoneal durante los últimos 15 años. Se evaluaron evolución clínica, infecciones del sitio de salida y del túnel, y los microorganismos causales y su sensibilidad, a fin de seleccionar la mejor terapia empírica para nuestro centro. Se realizaron dos procedimientos microbiológicos, método A: 100 ml del dializado fueron centrifugados y cultivados por métodos convencionales y en frascos para hemocultivo; método B: 10 ml fueron directamente inoculados en frascos para hemocultivo. Los hisopados del sitio de salida y del túnel fueron realizados cuando se observó supuración. Se registraron 96 episodios de peritonitis en 110,43 paciente-años (0,87 episodios/paciente-año). La sensibilidad del método A fue 96,88% *versus* 81,25% del método B (p = 0,001). La sensibilidad de la coloración de Gram fue 36,46%. La distribución de los agentes etiológicos fue la siguiente: 64 (56,64%) cocos gram-positivos, 22 (19,47%) bacilos gram-negativos fermentadores, 20 (17,7%) bacilos gram-negativos no fermentadores, 5 (4,43%) levaduras, 1 (0,88%) hongo micelial, 1 (0,88%) bacilo anaerobio. Fueron documentadas 55 infecciones del sitio de salida (0,5 episodios/paciente-año). La ceftazidima y el imipenem mostraron una excelente actividad sobre los bacilos gram-negativos. La sensibilidad a meticilina fue de 92,3% para *Staphylococcus aureus* y 33,3% para estafilococos coagulasa negativos; la vancomicina fue activa frente al 100% de los cocos gram-positivos. La evolución clínica de las peritonitis fue: 73 curas, 19 remociones de catéter y cuatro muertes relacionadas. La terapia empírica en nuestro centro debería ser vancomicina más ceftazidima o imipenem. Una vez conocidos el agente etiológico y su sensibilidad, se debería aplicar la terapia de desescalonamiento para evitar la emergencia y diseminación de microorganismos resistentes a la vancomicina.

Palabras clave: peritonitis, diálisis peritoneal, tasas de peritonitis, sitio de salida, infección del túnel

INTRODUCTION

In spite of technical advances such as improvement in catheter design and connection systems and the identification of risk factors, infectious peritonitis remains a leading cause of technique failure, hospitalization, damage of the peritoneal membrane and catheter loss, which contributes to the definitive drop-out and death of patients undergoing peritoneal dialysis therapy (6, 11, 15).

The development of disconnect systems and the introduction of the flush-before-fill twin bag system has had an important effect on overall reduction in the incidence of peritonitis episodes compared to the standard system (14), particularly, with the reduction in the incidence of gram-positive staphylococci and the increase of gram-negative rods.

The introduction of automated peritoneal dialysis (APD), using a single connection each night, showed a reduction in the incidence of peritonitis episodes compared with continuous ambulatory peritoneal dialysis (CAPD), as a result of the decrease in the number of daily disconnections (6, 10).

Since Gram staining of dialysate effluent has low diagnostic value, and bacterial cultures and drug susceptibility tests are time-consuming, most patients with peritonitis must be treated empirically (13).

Empiric therapy is controversial; the emergence of vancomycin-resistant enterococci has created a therapeutic dilemma because of the potential for transfer of the vancomycin resistance genes from enterococci to staphylococci. These events highlight the importance of finding ways to limit the spread of vancomycin-resistant enterococci (5).

The International Society for Peritoneal Dialysis (ISPD) Guidelines / Recommendations for Treatment of Peritoneal Dialysis - Related Peritonitis, discourage empiric therapy with vancomycin because of the emergence of vancomycin-resistant enterococci, and with gentamicin because of loss of residual renal function and ototoxicity. Therefore, cefazolin or cephalothin plus ceftazidime are recommended (9).

Despite recommendations, the route of antibiotic administration, duration of treatment, and initial choice of antibiotics differ from center to center (8, 9). Thus, the choice of initial empiric therapy should depend on each center's antibiotic profile, and those centers with high rate of methicillin-resistant organisms should use vancomycin. Subsequent antibiotic choice should depend on culture and susceptibility results (12).

This study reports the infectious peritonitis rates in three different systems, over the last 15 years, which includes clinical outcomes, exit-site infections, tunnel infections, causative microorganisms, and the history of susceptibility of organisms causing peritonitis in order to establish our center-specific selection of empiric therapy.

The design of this study was in accordance with the ethical standards of our Hospital Ethics Committee. Since the study was retrospective, informed consent was not required.

PATIENTS AND METHODS

Patients

Medical records of all patients undergoing peritoneal dialysis from January 1991 to December 2005 were retrospectively reviewed. The Manual-Spike method (SS), Twin bag disconnect system (YS) (Ultrabag^{TR}, Baxter^{R}, USA), and Automated Peritoneal Dialysis (APD) (Home choice automatic peritoneal dialysis system, Baxter^{R}, USA), were used during this period.

Forty four patients of 52.02 ± 20.10 years old (29 women and 15 men) with end-stage renal disease (ESRD) were included: 8 diabetes, 5 chronic glomerulonephritis, 2 chronic pyelonephritis, 3 systemic lupus erythematosus, 2 polycystic kidney diseases, 3 vesicoureteral reflux, 2 hemolytic-uremic syndrome, 2 intersticial nephritis, 1 branchio-oto-renal syndrome, 1 multiple myeloma, and 15 of unknown etiology. All patients were on peritoneal dialysis for > 30 days.

The willingness and the capability of the candidates were evaluated by pre-dialysis counselling. From 44 patients, 25 were satisfactorily selected but 19, in spite of a negative selection, were treated on peritoneal dialysis due to lack of vascular accesses or intolerance to hemodialysis. These patients were not good candidates for this treatment (negative selection).

Methods

All the episodes were studied and microbiologically documented according to method A) S. Vas with modifications (16): 100 ml of the dialysate were centrifuged at 3000 rpm for 15 minutes, the pellet was washed twice with phosphate-buffered saline, and resuspended in about 5 ml of it. Gram, Giemsa, and Ziehl Neelsen stains, and cultures on standard media were performed on the washed sediment: blood agar (Biokar Diagnostics, Beauvais, France), EMB Levine (Laboratorios Britania, CABA, Argentina), Sabouraud dextrose agar (home made) and brain heart infusion agar (Oxoid, Ltd, Basingstoke Hampshire, England) with 5% of sheep blood (Laboratorio Gutiérrez, CABA, Argentina), both the latter media with antibiotics, gentamicin and chloramphenicol (both from Sigma, St. Louis, USA) each one at 100 mg/l, incubated at both 28 and 35 °C; a CHROMagar™ Candida (Paris, France) was added when yeasts were seen through direct examination, thioglycolate medium (Difco/Becton Dickinson and Co, Sparks, Md., USA) and blood-culture bottle (until 2000, Hemo-100 Laboratorios Britania, CABA, Argentina, since 2001 aerobic blood culture bottle BD Standard/10 Aerobic/F, Becton Dickinson and Co, Sparks, Md., USA) were incubated up to 14 days at 35 °C. Method B) according to The British Society for Antimicrobial Chemotherapy (1): 10 ml were directly injected into blood-culture bottles.

When cultures with an elevate dialysate white blood cell (WBC) count were negative, cultures for *Mycobacterium tuberculosis* and other mycobacteria were done in solid media such as Lowenstein-Jensen and Stonebrink (both from Laboratorios Britania, CABA, Argentina), and a liquid medium such as BD Myco/F lytic (Becton Dickinson and Co, Sparks, Md., USA).

Swabs from the exit site or tunnel were taken when purulent drainage or erythema were observed.

Susceptibility testing was performed on 95 isolates, kept frozen at - 70 °C in 15% glycerol broth: 26 *Staphylococcus aureus*, 27 coagulase-negative staphylococci (CNS), 22 gram-negative fermentative rods (GNFR) and 20 gram-negative non-fermentative rods (GNNFR) by using the Clinical and Laboratory Standards Institute methods (CLSI) (3). Mueller-Hinton agar (Difco/Becton Dickinson and Co, Sparks, Md., USA) was used and serial twofold dilutions of antimicrobial agents were reconstituted according to the manufacturers´ instructions on the day of the test and added to the media. Reagent grade powders of oxacillin and vancomycin were purchased from Sigma-Aldrich (St. Louis, USA), and the following were obtained from their manufacturers in Argentina: teicoplanin (Aventis-Pharma), linezolid (Pfizer), imipenem (Merck, Sharp & Dohme), gentamicin (Bagó), ciprofloxacin (Laboratorio Roemmers), mupirocin and ceftazidime (Glaxo, Smith-Kline), amikacin and cephalotin (Bristol-Meyers Squibb), and cotrimoxazole (Roche).

Agar plates were inoculated with a Steers replicator. The inoculum used was 10^4 CFU per spot. The plates were incubated at 35 °C for 24h and then examined.

The rapid latex agglutination test (Slidex MRSA Detection test, bioMérieux Marcy l´Étoile-France) detecting methicillin resistance in staphylococci was performed according to the manufacturer's instructions and with the modification proposed by A. Corso *et al.* (4).

The initial empiric antibiotic selection was according to the recommendations of the International Society of Peritoneal Dialysis (8, 9, 12). Once the organisms were identified and the susceptibility pattern determined, appropriate adjustments in antibiotics were made.

Case definition

Peritonitis definition includes at least two of the following criteria: a) abdominal pain or tenderness, b) cloudy drainage fluid, with WBC count greater than 100/mm^3, with at least 50% neutrophils, and c) a positive culture (and/or Gram stain) of the dialysate. Culture-negative cases were included in the total number of episodes of infectious peritonitis, but excluded from all subsequent analysis. Outcome was classified as initial cure, catheter removal or patient's death.

Initial cure was defined as the resolution of peritonitis evidence with antimicrobial therapy and without the need of catheter removal. Deaths related to infectious peritonitis were considered when the patients died within 4 weeks of presentation of peritonitis.

Terminology for exit-site and tunnel infections, refractory, recurrent, relapsing, and repeat peritonitis, and catheter-related peritonitis were used according to ISPD Guidelines/Recommendations (12).

Statistical methods

Patients' demographics and comparisons of peritonitis rates were analyzed using the chi-square test. A p value less than or equal to 0.05 was considered significant.

RESULTS

There were 96 episodes of peritonitis during 110.43 patient-years, which yielded an overall incidence of peritonitis of 0.87 episodes/patient-year. Table 1 shows permanence of patients on peritoneal dialysis, number of infectious peritonitis episodes, peritonitis rates, and etiology in the three different methods. A reduction of the peritonitis rates was observed in APD and YS with respect to SS ($p < 0.001$), however the difference was not statistically significant between APD and YS ($p = 0.906$). A marked reduction in the incidence of gram-positive cocci and an increase of gram-negative rods were seen in APD with respect to SS ($p < 0.001$), and YS (p = 0.004).

Figure 1 shows the global peritonitis rate over the past 15 years. The SS was used from 1991 to 1996, the YS began in 1994, and since 1996 all patients have been treated by YS and/or APD.

The distribution of global peritonitis rate/patient, frequency and mean are showed in Table 2. Twenty-one patients (47.73%) experienced between 0 to 0.5 episodes/

Table 1. Permanence of patients on peritoneal dialysis, number of infectious peritonitis episodes (IP), peritonitis rates (PR), and etiology in the three different methods.

Method	Years	IP	PR(1)	GPC %	GNR %	Yeasts %	Micelial fungi %
SS	21.61	35	1.61	63.41	31.71	4.88	0
SY	66.78	46	0.69	55.93	37.29	5.08	1.69
APD	22.04	15	0.68	38.46	61.54	0	0
Total	110.43	96	0.87	56.63	38.05	4.42	0.88

(1) PR are expressed as episodes per patient-year.
GPC: gram-positive cocci; GNR: gram-negative rods.

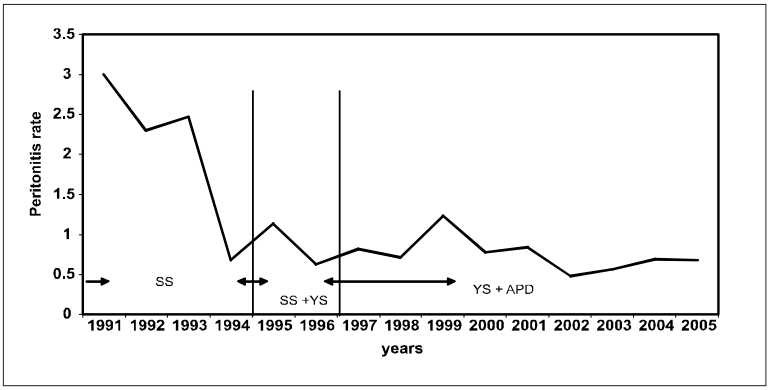

Figure 1. Global peritonitis rate over the last 15 years.
SS: Manual-Spike method, YS: Doble bag disconnect system, APD: Automated peritoneal dialysis.

patient-year, and only two patients had 3 to 4 episodes/patient-year.

The peritonitis rate from 25/44 patients satisfactorily selected for the treatment was 0.62 episodes/patient-year *versus* 1.27 episodes/patient-year from 19 patients treated with peritoneal dialysis because of lack of other therapeutic option (negative selected group) ($p = 0.038$).

All peritoneal fluids were cloudy or partially cloudy with an average WBC count of 2,602 ± 293/mm^3 (range, 120-10,700/mm^3). In 93/96 episodes, the etiologic agent was isolated resulting in a sensitivity of 96.88% of culture method A *versus* 81.25% (78/96) of method B (p= 0.001), whereas the overall Gram stain sensitivity was 36.46%.

Eighty one episodes had only one microorganism (87.1%) and 12 of them (12.9%) had ≥ 2.

The etiologic agents were: 64 (56.64%) gram-positive cocci, 22 (19.47%) gram-negative fermentative rods, 20 (17.7%) gram-negative nonfermentative rods, 5 (4.43%) yeasts, 1 (0.88%) micelial fungus, and 1 (0.88%) anaerobic rod. Table 3 shows the microorganisms isolated in the 93 episodes of peritonitis.

Fifty-five exit-site infections were documented. The infection rate was 0.5 episodes/patient-year. From a total of 96 episodes of infectious peritonitis only 6 (6.25%) were related to the exit-site infection. The microorganisms isolated were: 4 methicillin-susceptible *Staphylococcus aureus* (MSSA) and 1 methicillin-resistant *Staphylococcus aureus* (MRSA), 1 *Proteus mirabilis*, and 1 *Pseudomonas pseudoalcaligenes.* Only one tunnel infection due to *Pseudomonas aeruginosa* was recorded during this period.

There were eight refractory peritonitis caused by: 3 MSSA, 2 *Candida albicans*, 1 *Candida glabrata*, 1 *Neosartorya hiratsukae*, and 1 *Methylobacterium fujisawaense* and nine relapsing peritonitis caused by: 3 *S. aureus* (2 MSSA, 1 MRSA), 2 methicillin-resistant *Staphylococcus epidermidis*, 1 methicillin-susceptible *Staphylococcus warneri*, 1 *C. albicans,* 1 *P. pseudoalcaligenes,* and one of polimicrobian etiology. All catheters were removed.

Six recurrent and two repeat peritonitis were recorded, the latter caused by *P. aeruginosa* and a MSSA, respectively. Both catheters were removed.

Table 4 shows the *in vitro* susceptibility of 53 gram-positive cocci and 42 gram-negative rods. Ceftazidime and imipenem showed excellent activity on gram-negative rods, 100% on GNFR and 95% on GNNFR. Ciprofloxacin showed high efficacy against overall microorganisms including 96.2% of *S. aureus,* 92.6% of CNS, 90.9% of GNFR, and 90% of GNNFR.

All gram-positive cocci were susceptible to vancomycin, and 92.3% of *S. aureus* but only 33.3% of CNS were susceptible to methicillin. Methicillin resistance was investigated in 53 staphyloccoci isolates through the detection of the penicillin-binding-protein 2 a (PBP2a), which resulted positive in 20 (38%) of the isolates, 2 *S. aureus* and 18 CNS. Figure 2 shows the distribution of methicillin resistance over the last 15 years.

The clinical outcome of peritonitis was: 73 initial cure, 19 catheter removal and four deaths. Over this 15 year-period, the initial cure rate was 76%, the catheter removal rate 19.8% and the associated infectious peritonitis death rate was 4.16%.

During this period, out of 44 patients, 13 were transferred to hemodialysis (four due to poor ultrafiltration), six were transplanted, 13 died (four related to the infectious peritonitis episode), and 12 continued on peritoneal dialysis.

DISCUSSION

Since 1979, continuous ambulatory peritoneal dialysis was established in our hospital as treatment of patients with ESRD. Between January 1981 and June 1988, 18 patients with standard method experienced 80 episodes during 17 patient-years yielding a very high overall peritonitis rate of 4.7 episodes/patient-year (13).

In this study, from January 1991 to December 2005 a great reduction in the global infectious peritonitis rate was observed (0.87 episodes/patient-year), with respect to

Table 2. Distribution of peritonitis rates (PR).

Range PR	Nº of patients	%	Mean	Standard deviation
0 to 0.5	21	47.73	0.18	0.1906
0.5 to 1	6	13.64	0.69	0.1628
1 to 1.5	7	15.91	1.31	0.0697
1.5 to 2	6	13.64	1.78	0.1590
2 to 2.5	2	4.55	2.22	0.2333
2.5 to 3	0	0	-	
3 to 3.5	1	2.27	3.03	
3.5 to 4	1	2.27	3.66	
Total	44	100	0.87	0.8842

Table 3. Microorganisms isolated in 93 episodes of peritonitis.

Gram-positive cocci	n (%)
Staphylococcus aureus	26
Staphylococcus epidermidis	22
Staphylococcus haemolyticus	3
Staphylococcus warneri	1
Staphylococcus caprae	1
Enterococcus faecium	2
Enterococcus hirae	1
Streptococcus parasanguinis	2
Streptococcus pasteurianus	1
Streptococcus agalactiae	1
Streptococcus mutans	1
Streptococcus sanguinis biotype 1	1
Streptococcus mitis	1
Streptococcus salivarius	1
Total	64 (56.64)

Gram-negative fermentative rods	n (%)
Escherichia coli	6
Klebsiella pneumoniae	4
Enterobacter cloacae	2
Klebsiella oxytoca	2
Citrobacter freundii	1
Proteus mirabilis	1
Proteus vulgaris	1
Serratia marcescens	1
Enterobacter agglomerans	1
Salmonella enteritidis	1
Yokenella regensburgei	1
Methylobacterium fujisawaense	1
Total	22(19.47)

Gram-negative non-fermentative rods	n (%)
Pseudomonas aeruginosa	9
Pseudomonas pseudoalcaligenes	3
Pseudomonas fluorescens	1
Pseudomonas alcaligenes	1
Pseudomonas grupo 1	1
Acinetobacter baumannii	2
Burkholderia cepacia complex	1
Psychrobacter immobilis	1
Sphingomonas paucimobilis	1
Total	20 (17.70)

Anaerobes	n (%)
Bacteroides vulgatus	1
Total	1(0.88)

Yeasts	n (%)
Candida albicans	3
Candida glabrata	1
Candida parapsilosis	1
Total	5 (4.43)

Micelial fungi	n (%)
Neosartorya hiratsukae	1
Total	1(0.88)

Table 4. *In vitro* susceptibility of 53 gram-positive cocci and 42 gram-negative rods isolated from peritonitis episodes.

Antibiotic	SA MIC_{90}	n = 26 S (%)	CNS MIC_{90}	n = 27 S (%)	GNFR MIC_{90}	n = 22 S (%)	GNNFR MIC_{90}	n = 20 S (%)
Oxacillin	1	92.3	32	33.3	–	–	–	–
Vancomycin	0,5	100	4	100	–	–	–	–
Teicoplanin	0,5	100	4	100	–	–	–	–
Ciprofloxacin	0,5	96.2	0,5	92.6	0,25	90.9	1	90
Gentamicin	64	72	32	29.6	≤ 1	95.4	> 128	60
Amikacin	8	92.3	8	100	≤ 2	100	> 256	65
Cotrimoxazole	≤ 0.063	100	4	81.5	0,5	86.4	> 128	50
Linezolid	1	100	0,5	100	–	–	–	–
Mupirocin	≤ 0.125	96	0,063	100	–	–	–	–
Imipenem	–	–	–	–	≤ 1	100	≤ 1	95
Ceftazidime	–	–	–	–	≤ 2	100	4	95
Cephalotin	–	–	–	–	128	68	–	–

SA: *Staphylococcus aureus*; CNS: coagulase-negative staphylococci; GNFR: gram-negative fermentative rods; GNNFR: gram-negative non-fermentative rods; MIC: minimal inhibitory concentration; S: susceptibility; cotrimoxazole: trimethoprim-sulfamethoxazole.

what was previously reported; nevertheless, when we analyzed the distribution of peritonitis in range every six-months, in 47.73% of patients the infectious peritonitis rate was 0.18 episodes/patient-year.

Our results showed a marked decrease in the peritonitis rate in APD (0.68 episodes/patient-year) and in YS (0.69 episodes/patient-year) *versus* SS (1.61 episodes/patient-year). The following advantages could be related to these results: a reduction in the number of daily disconnections, the improvement of the method with the flush-before-fill system, and the creation of teams of specialized nurses and nephrologists with specific experience, who trained and followed the patients in a special sector of the nephrology center. All patients satisfactorily selected for the treatment had lower peritonitis rates than those negatively selected.

There was no statistically significant difference between the peritonitis rates in APD compared to YS, in spite of the lower number of daily disconnections. Kavanagh *et al.* (7) showed similar results. All our patients treated with APD belong to the negatively selected group.

The decrease in the incidence of gram-positive cocci in APD could be related to the lower number of connections and the flush-before-fill system, and it could lead to a higher relative incidence of gram-negative peritonitis.

The centrifugation of 100 ml of dialysate and washed sediments showed an excellent recovery of microorganisms with a sensitivity of 96.88% (93/96 episodes), exceeding the rate for positive cultures by more than 90% (1, 12). The direct inoculation of 10 ml of dialysate in blood-culture bottles showed good recovery with a sensitivity of 81.25% (78/96), with less than 20% of negative cultures. Although this value of sensitivity is still accepted by the ISPD Guidelines / Recommendations (12), there was a statistically significant difference (p = 0.001) when both methods were compared.

The “Recommended Standards for the Treatment of Adult Patients with Renal Failure” from The Renal Association and The Royal College of Physicians stated that less than 10% of all episodes of PD peritonitis should be culture negative in 1997, and fewer than 15% in 2002 (7).

The overall Gram stain sensitivity was low (36.46%). In the study carried out between January 1981 and June 1988 we obtained a Gram sensitivity of 49.3% with the centrifugation of all the peritoneal dialysis effluent (13). Since Gram sensitivity continue to be low, the correct microbiological culture is necessary to establish the etiological agent and the appropriate antibiotic therapy according to the susceptibility pattern.

Most episodes had only one microorganism (87.1%), and 12 (12.9%) were of polimicrobian etiology, probably, by spontaneous or secondary peritonitis. *Bacteroides vulgatus* was the only anaerobic rod isolated (0.88%) in one episode in a patient with diverticulitis and amyloidosis.

A variety of opportunistic pathogens was isolated among the peritonitis etiologic agents as it was shown in Table 3, with unusual isolates such as *Methylobacterium fujisawaense*, and *Neosartorya hiratsukae* related, in both cases, to an exogenous origin of the primary peritonitis resulting from direct contamination of the connection device.

CNS were the first cause of peritoneal dialysis-related peritonitis followed by *S. aureus,* and in most cases, they were the result of catheter contamination from a colonized patient.

We found an exit-site infection rate of 0.5 episodes/patient-year, and only 6/96 (6.25%) of the peritonitis episodes were due to the exit-site infection. Burkart *et al.* (2) found exit-site infection rates between 0.26 and 0.62 depending on the connection system used. Only one tunnel infection was recorded during the period.

All catheters were removed from nine relapsing, eight refractory, and two repeat peritonitis, to protect the peritoneal membrane for future use.

The finding in 1997 of vancomycin-resistant *Enterococcus faecium* in the peritoneal fluid of one of our patients, and the 1996 update of the ISPD which was rather controversial because vancomycin was changed by cefazolin or cephalothin in the initial empiric antibiotic scheme, led us to evaluate our own center´s antibiotic profile (Table 4).

The history of susceptibilities of organisms causing peritonitis in our center showed for gram-negative coverage that ceftazidime and imipenem had an excellent activity against the gram-negative rods, over 100% of GNFR and 95% of GNNFR.

Ciprofloxacin was the third most active drug against 90.9% of GNFR and 90% of GNNFR, while aminoglycosides, cephalotin and trimethoprim-sulfamethoxazole were not good therapeutic options.

Gram-positive staphylococci including 26 *S. aureus* and 27 CNS isolates were susceptible to vancomycin. Cefazolin or cephalothin susceptibilities were inferred through oxacillin susceptibility and by the detection of PBP2a, with 92.3% of *S. aureus* and 33.3% of CNS susceptibility. We observed a low number of methicillin-resistant staphylococci in the period studied, except in 1991 (3 CNS), 1994 (3 CNS) and in 1997 (4 CNS and 1 *S. aureus*), as shown in Figure 2. There were 40 infectious peritonitis episodes between 1998 and 2005 with 5 due to MR-CNS (12.5%), therefore, the gram-positive coverage in our center must include vancomycin.

The initial cure rate over 15 years was low (76%) compared to several large outcome studies that showed cure with eradication of the infection in 80-85% of peritonitis episodes. The catheter removal rate was 19.8% in comparison with approximately 10-15%, and the death rate was 4.16%, while others showed 1 to 6% (15).

In summary, peritonitis continues to be the leading cause of technique failure of peritoneal dialysis in our hospital.

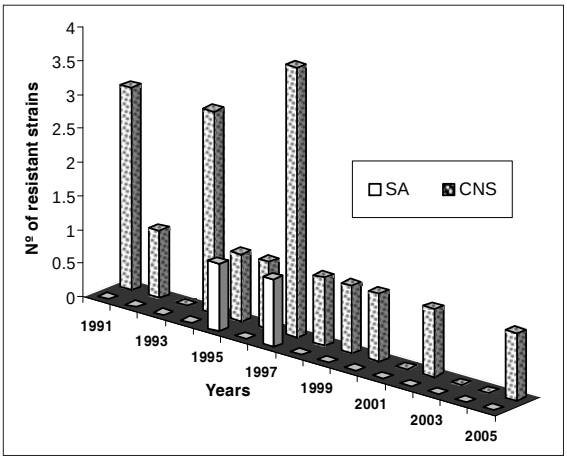

Figure 2. Distribution of methicillin resistance in *S. aureus* and CNS over the last 15 years

The centrifugation of 100 ml of dialysate showed the highest sensitivity (96.88%) in the recovery of microorganisms.

Our results suggest that prior to knowledge of the causative agent, the empiric therapy in our center should be vancomycin plus ceftazidime or imipenem. Once the etiological agent and its susceptibility are known, the de-escalating therapy must be applied, and if an *S. aureus* or CNS methicillin-susceptible is confirmed, vancomycin must be immediately discontinued and replaced by a first generation cephalosporin to avoid the emergence and spread of vancomycin-resistant microorganisms.

REFERENCES

1. Bint AJ, Finch RG, Gokal R, Goldsmith HJ, Oliver BD Jr. Diagnosis and management of peritonitis in continuous ambulatory peritoneal dialysis. Report of a working party of the British Society for Antimicrobial Chemotherapy. Lancet 1987; 1: 845-8.
2. Burkart JM, Jordan JR, Durnell TA, Case LD. Comparison of exit-site infections in disconnect versus nondisconnect systems for peritoneal dialysis. Perit Dial Int 1992; 12: 317-20.
3. Clinical and Laboratory Standards Institute. MIC testing. Performance standards for antimicrobial susceptibility testing; 16th informational supplement, 2006; M100-S16. Wayne, Pa, USA.
4. Corso A, Soloaga R, Faccone D, Gagetti P, Corbella S, Iglesias M, *et al*. Improvement of a latex agglutination test for the evaluation of oxacillin resistance in coagulase-negative staphylococci. Diag Microbiol Inf Dis 2004; 50: 223-5.
5. Donskey CJ, Rice LB. The influence of antibiotics on spread of vancomycin-resistant enterococci: the potential role of selective use of antibiotics as a control measure. Clin Microbiol News 1999; 21: 57-65.
6. Huang JW, Hung KJ, Yen CJ, Wu KD, Tsai TJ. Comparison of infectious complications in peritoneal dialysis patients using either a twin-bag system or automated peritoneal dialysis. Nephrol Dial Transplant 2001; 16: 604-7.
7. Kavanagh D, Prescott GJ, Mactier, RA. Peritoneal dialysis-associated peritonitis in Scotland (1999-2002). Nephrol Dial Transplant 2004; 19: 2584-91.
8. Keane WF, Alexander SR, Bailie GR. Peritoneal dialysis-related peritonitis treatment recommendations: 1996 update. Perit Dial Int 1996; 16: 557-73.
9. Keane WF, Bailie GR, Boeschoten E, Gojal R, Golper TA, Holmes CJ, *et al*. Adult peritoneal dialysis related peritonitis treatment recommendations: 2000 update. Perit Dial Int 2000; 20: 396-411.
10. Locatelli AJ, Marcos GM, Gomez MG, Alvarez SA, De Benedetti LC. Comparing peritonitis in continuous ambulatory peritoneal dialysis patients versus automated peritoneal dialysis patients. Adv Perit Dial 1999; 15: 193-6.
11. Piraino B. Infectious complications of peritoneal dialysis. Perit Dial Int 1997; 17 Suppl 3: S15-8.
12. Piraino B, Bailie GR, Bernardini J, Boeschoten E, Gupta A, Holmes C, *et al*. Peritoneal dialysis-related infections recommendations: 2005 update. Perit Dial Int 2005; 25: 107-31.
13. Predari SC, Abalo AB, Santoianni JE, Prado A, Ribas MC, Zucchini A. Peritonitis en diálisis peritoneal continua ambulatoria. Evaluación microbiológica y clínica. Medicina (Buenos Aires) 1990; 50: 102-6.
14. Strippoli GF, Tong A, Johnson D, Schena FP, Craig JC. Catheter-related interventions to prevent peritonitis in peritoneal dialysis: a systematic review of randomized, controlled trials. J Am Soc Nephrol 2004; 15: 2735-46.
15. Troidle L, Finkelstein F. Treatment and outcome of CPD-associated peritonitis. Ann Clin Microbiol Antimicrob 2006; 5: 6 (available www.ann-linmicrob.com/content/5/1/6).
16. Vas SI. Microbiologic aspects of chronic ambulatory peritoneal dialysis. Kidney Int 1983; 23: 83-92.

Recibido: 17/7/07 – Aceptado: 6/11/07