Peritoneal Dialysis International, Vol. 24, pp. 424–432
Printed in Canada.

0896-8608/04 $3.00 + .00

REVIEWS AND ORIGINAL ARTICLES

CHANGES IN CAUSATIVE ORGANISMS AND THEIR ANTIMICROBIAL SUSCEPTIBILITIES IN CAPD PERITONITIS: A SINGLE CENTER'S EXPERIENCE OVER ONE DECADE

Dong Ki Kim,[1] Tae-Hyun Yoo,[1] Dong-Ryeol Ryu,[1] Zhong-Gao Xu,[1] Hyun Jin Kim,[1] Kyu Hun Choi,[1] Ho Yung Lee,[1] Dae-Suk Han,[1,2] and Shin-Wook Kang[1,2]

Department of Internal Medicine,[1] Yonsei University College of Medicine; Institute of Kidney Disease,[2] Brain Korea 21, Yonsei University, Seoul, Korea

♦ ***Background:*** **In recent years, the rate of peritonitis during continuous ambulatory peritoneal dialysis (CAPD) has been significantly reduced. However, peritonitis remains a major complication of CAPD, accounting for considerable mortality and hospitalization among CAPD patients.**

♦ ***Objective:*** **To generate a "center tailored" treatment protocol for CAPD peritonitis by examining the changes of causative organisms and their susceptibilities to antimicrobial agents over the past 10 years.**

♦ ***Method:*** **Retrospective review of the medical records of 1015 CAPD patients (1108 episodes of peritonitis) who were followed up from 1992 through 2001.**

♦ ***Results:*** **The overall incidence of peritonitis was 0.40 episodes/patient-year. The annual rate of peritonitis and the incidence of peritonitis caused by a single gram-positive organism were significantly higher in 1992 and 1993 compared with those in the rest of the years ($p < 0.05$). The incidence of peritonitis due to coagulase-negative staphylococcus (CoNS) decreased significantly over time, whereas there was no significant change in the incidence of *Staphylococcus aureus* (SA)-induced peritonitis. Among CoNS, resistance to methicillin increased from 18.4% in 1992 – 1993 to 41.7% in 2000 – 2001 ($p < 0.05$). In contrast, the incidence of methicillin-resistant SA was not different according to the calendar year. Catheter removal rates were significantly higher in peritonitis due to a single gram-negative organism (16.6%) compared with gram-positive peritonitis (4.8%, $p < 0.005$). The mortality associated with peritonitis was also higher in gram-negative (3.7%) compared with gram-positive peritonitis (1.4%), but there was no statistical significance. Among single gram-positive organism-induced peritonitis, catheter removal rates were significantly higher in SA (9.3%) than those in CoNS (2.9%, $p < 0.01$) and other gram-positive organisms (2.9%, $p < 0.05$). In peritonitis caused by CoNS, the methicillin-resistant group showed significantly higher removal rates than the methicillin-susceptible group (8.2% vs 1.0%, $p < 0.01$).**

♦ ***Conclusion:*** **The incidence of peritonitis for 2001 decreased to less than half that for 1992, due mainly to a significant decrease in CoNS-induced peritonitis, whereas the proportions of peritonitis due to a single gram-negative organism and methicillin-resistant CoNS increased. These findings suggest that it is necessary to prepare new center-based guidelines for the initial empirical treatment of CAPD peritonitis.**

Perit Dial Int **2004; 24:424–432** **www.PDIConnect.com**

KEY WORDS: Peritonitis; gram-positive organism; gram-negative organism; antimicrobial susceptibility; coagulase-negative staphylococcus; *Staphylococcus aureus*.

Peritonitis is not only a common complication in end-stage renal disease (ESRD) patients treated with continuous ambulatory peritoneal dialysis (CAPD), but also is the leading cause of transfer to hemodialysis (1–4). Although the incidence of peritonitis varies from center to center, it decreased dramatically in the 1990s to 1 episode/24 patient-months (5–8).

The development of disconnect systems has significantly reduced the overall incidence of peritonitis (6–10), especially those caused by coagulase-negative

Correspondence to: S.-W. Kang, Department of Internal Medicine, Yonsei University College of Medicine, 134 Shinchon-Dong Seodaemoon-Gu, Seoul, 120-752, Korea.
kswkidney@yumc.yonsei.ac.kr
Received 16 December 2003; accepted 24 March 2004.

staphylococcus (CoNS), the major organism responsible for touch contamination. However, the incidence of peritonitis caused by gram-negative organisms remains at a steady level; therefore, their proportion has increased relatively (11–14).

The character of a causative organism is an important determinant of clinical outcome (12,15–17). Widely used treatment guidelines have continually been modified by the International Society for Peritoneal Dialysis (ISPD), the most recent modification being made in 2000 (18). Treatment guidelines should be changed depending on the causative organisms because empirical antimicrobial regimens for peritonitis are established by the major causative organisms. Even though cross-sectional studies on the causative organisms of peritonitis have been reported frequently, long-term studies on changes in the causative organisms of peritonitis are scarce (11,12). There has been only one study, conducted at a single center, that analyzed the changes in infecting pathogens and also their antimicrobial sensitivities (13).

In the present study, we investigated the causative organisms, antimicrobial susceptibility, and catheter removal rates relative to the causative organisms in 1015 CAPD patients with peritonitis, who were followed up at Severance Hospital, Seoul, between 1992 and 2001. Yearly changes in the causative organisms and antimicrobial susceptibility of each causative organism were also examined.

METHODS

This retrospective study was conducted with the medical records of 1015 CAPD patients who were followed up from January 1992 to December 2001 at Severance Hospital, Yonsei University College of Medicine, Seoul, Korea. All the patients were on CAPD with a double-cuffed, straight Tenckhoff catheter. Catheters were placed by a nephrologist, using a Tenckhoff trocar, at the lateral border of the rectus muscle; the skin exit was made at the counterpoint of the catheter insertion site in a downward direction. After catheter placement, intraperitoneal cefazolin for 3 days was routinely used.

The data recorded included age at time of peritonitis, age at start of CAPD, sex, cause of ESRD, causative organisms of peritonitis, antimicrobial susceptibility of each organism, and date of catheter removal. Patients were classified as having peritonitis if they satisfied at least two of the following criteria (6): (1) presence of clinical symptoms (pain, fever, cloudy dialysate); (2) presence of more than 100 leukocytes/mm^3 dialysate, with at least 50% polymorphonuclear neutrophils; and (3) positive culture or Gram stain. An episode of peritonitis within 4 weeks after the treatment of a previous episode was considered a relapse and was not classified as a new infection. In addition, a peritonitis episode within 7 days after catheter placement was also excluded.

Since November 1993, culture of the dialysate has been performed as recommended by the ISPD (19). Whole dialysate (50 mL) is concentrated by centrifugation, resuspended in sterile saline, inoculated into blood culture media, and observed for at least 72 hours to document pathogens. Antimicrobial susceptibility is determined by standard disk-diffusion method.

For the present study, the causative organisms of peritonitis were divided into gram-positive organisms (*Staphylococcus aureus*, CoNS, *Streptococcus*, and *Enterococcus*), gram-negative organisms (*Escherichia coli*, *Pseudomonas aeruginosa*, other *Pseudomonas spp*, *Acinetobacter*, *Serratia*, *Klebsiella*, *Enterobacter*, and other gram-negative organisms), multi-organisms, fungi, *Mycobacterium tuberculosis*, and culture negative.

The numbers and rates of peritonitis were calculated per year of the entire study period. The numbers, incidences, and proportions of peritonitis due to gram-positive organisms, gram-negative organisms, multi-organisms, fungi, *M. tuberculosis*, and culture-negative peritonitis in each year were quantified. In addition, the numbers, incidences, and proportions of peritonitis caused by gram-positive organisms and gram-negative organisms were analyzed according to the duration of CAPD before the onset of peritonitis: 1 – 6 months, 7 – 12 months, 13 – 18 months, 19 – 24 months, 25 – 36 months, 37 – 48 months, 49 – 60 months, 61 – 72 months, 73 – 96 months, and ≥ 97 months.

Among gram-positive organisms, *S. aureus* was divided into methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) groups; CoNS was also divided into methicillin-susceptible and -resistant groups. The numbers, incidences, and proportions of peritonitis caused by each group were then compared for every 2 years of the 10-year study period. *Enterococcus* species were divided into *E. faecalis* and *E. faecium*, and their susceptibilities to ampicillin and vancomycin were investigated. Gram-negative organisms were divided into *E. coli*, *P. aeruginosa*, and other gram-negative organisms, and the antimicrobial susceptibilities to aminoglycoside (tobramycin, gentamicin, and amikacin), quinolone, and imipenem were analyzed for each organism.

When peritonitis was diagnosed, empirical therapy with a combination of cefazolin and tobramycin was initiated. Within 72 hours, the empirical antibiotics were adjusted based on the results of the dialysate culture and antimicrobial susceptibility test. In culture-negative peritonitis with no response to initial therapy after 72 hours, cefazolin and tobramycin were substituted by vancomycin and amikacin. If peritonitis did not respond to adequate antibiotics after

96 hours, the catheter was removed. In addition, the catheter was removed in cases of frequent relapsing peritonitis, fungal peritonitis, and tuberculous peritonitis.

The catheter removal rates in peritonitis were calculated according to the causative organisms: gram-positive organisms, gram-negative organisms, fungi, *M. tuberculosis*, and culture negative. In addition, the catheter removal rates were compared for each organism according to its antimicrobial susceptibility.

STATISTICAL ANALYSIS

Data are expressed as episodes/patient-year, percent, and mean ± standard deviation (SD). The incidence of peritonitis was compared using the Poisson regression model (20). Differences in the proportion of causative organisms were analyzed according to each calendar year. Antimicrobial susceptibilities and catheter removal rates according to the pathogens were analyzed using chi-square analysis or Fischer's exact test. Statistical significance was determined as p value less than 0.05.

RESULTS

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS (TABLE 1)

Of the 1015 patients examined, 537 were men and 478 were women, their mean age at the initiation of CAPD was 50.7 ± 13.6 years, and they were followed up for a mean period of 3.3 ± 2.6 years. The causes of ESRD are listed in Table 1.

CAUSATIVE ORGANISMS OF PERITONITIS

A total of 1108 episodes of peritonitis were recorded during this 10-year study period. The causative organisms of peritonitis are listed in Table 2.

TABLE 1
Clinical Characteristics of Patients

Patients (*n*)	1015
Sex (male:female)	537:478
Age (years)	50.7±13.6[a]
Mean duration of follow-up (years)	3.3±2.6
Underlying disease [*n* (%)]	
Chronic glomerulonephritis	328 (32.3)
Diabetes mellitus	326 (32.1)
Hypertension	149 (14.7)
Polycystic kidney disease	24 (2.4)
Systemic lupus erythematosus	12 (1.2)
Others or unknown	176 (17.3)

[a] Mean ± standard deviation.

TABLE 2
Causative Organisms of CAPD Peritonitis (*n* = 699)

Organisms	*N* (%)
Gram positives	498 (71.2)
CoNS	279 (39.9)
Staphylococcus aureus	151 (21.6)
Streptococcus sp	55 (7.9)
Enterococcus sp	13 (1.9)
Gram negatives	163 (23.3)
Escherichia coli	60 (8.6)
Pseudomonas aeruginosa	32 (4.6)
Other *Pseudomonas* species	5 (0.7)
Acinetobacter sp	18 (2.6)
Klebsiella sp	13 (1.9)
Serratia sp	9 (1.3)
Enterobacter sp	8 (1.1)
Other gram negatives	18 (2.6)
Multi-organism	13 (1.9)
Fungi	24 (3.4)
Mycobacterium tuberculosis	1 (0.1)

CoNS = coagulase-negative staphylococcus.

Single gram-positive organisms caused 498 episodes of peritonitis (44.9%), single gram-negative organisms caused 163 episodes (14.7%), multi-organisms caused 13 episodes (1.2%), fungi caused 24 episodes (2.2%), and *M. tuberculosis* caused 1 episode (0.1%). There were 409 episodes (36.9%) of culture-negative peritonitis. When culture-negative episodes were excluded, the most cases (71.2%) of peritonitis were caused by a single gram-positive organism: 39.9% by CoNS, 21.6% by *S. aureus*, 7.9% by *Streptococcus*, and 1.9% by *Enterococcus*. Single gram-negative organisms accounted for 23.3% of culture-positive peritonitis: *E. coli* in 8.6%, *P. aeruginosa* in 4.6%, other *Pseudomonas spp* in 0.7%, *Acinetobacter* in 2.6%, *Klebsiella* in 1.9%, *Serratia* in 1.3%, *Enterobacter* in 1.1%, and other gram-negative organisms in 2.6%.

PERITONITIS RATES AND CAUSATIVE ORGANISMS ACCORDING TO EACH CALENDAR YEAR

The overall incidence of peritonitis during the 10-year study period was 0.40 episodes/patient-year. When the incidence of peritonitis was analyzed according to each calendar year, it was significantly decreased (to < 0.40 episodes/patient-year) after 1998. Compared with 1992 and 1993, the incidence of peritonitis due to a single gram-positive organism decreased significantly after 1994 ($p < 0.05$), whereas that of gram-negative peritonitis increased, resulting in a significant increase in the proportion of gram-negative peritonitis after 1994 ($p < 0.05$) (Table 3 and Figure 1). This decrease in the incidence of peritoni-

TABLE 3
Incidences and Causative Organisms of CAPD Peritonitis from 1992 to 2001

Year	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
CAPD patients (*n*)	203	265	324	347	395	432	466	506	495	498
Mean age (years)	49.0	48.9	49.1	50.2	51.5	52.7	53.7	55.0	56.0	56.2
Patients on double bag (%)	36.9	62.3	91.0	95.1	97.5	97.7	98.7	98.8	98.8	99.0
Diabetics (%)	25.6	22.6	22.2	22.8	22.8	24.0	24.4	27.2	27.0	26.1
Peritonitis episodes (*n*)	81	86	97	121	152	129	125	136	95	86
Incidence (episodes/patient-year)	0.49	0.50	0.48	0.42	0.45	0.45	0.34	0.35	0.25	0.23
Culture negative [*n* (%)]	26 (32.1)	23 (26.7)	27 (27.8)	54 (44.6)	71 (46.7)	37 (28.7)	45 (36.0)	56 (41.2)	38 (40.0)	32 (37.2)
Organisms [*n* (%)]										
Gram positive	48 (87.3)	56 (88.9)	47 (67.1)	46 (68.7)	59 (72.8)	63 (68.5)	50 (62.5)	49 (61.3)	42 (73.7)	38 (70.4)
Gram negative	4 (7.3)	6 (9.5)	17 (24.3)	16 (23.9)	19 (23.5)	22 (23.9)	23 (28.8)	29 (36.3)	12 (21.1)	15 (27.8)
Multi-organism	2 (3.6)	0 (0)	2 (2.9)	1 (1.5)	2 (2.5)	2 (2.2)	2 (2.5)	0 (0)	1 (1.8)	1 (1.9)
Fungi	1 (1.8)	1 (1.6)	3 (4.3)	4 (6.0)	1 (1.2)	5 (5.4)	5 (6.3)	2 (2.5)	2 (3.5)	0 (0)
Mycobacterium tuberculosis	0 (0)	0 (0)	1 (1.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total	55 (100)	63 (100)	70 (100)	67 (100)	81 (100)	92 (100)	80 (100)	80 (100)	57 (100)	54 (100)

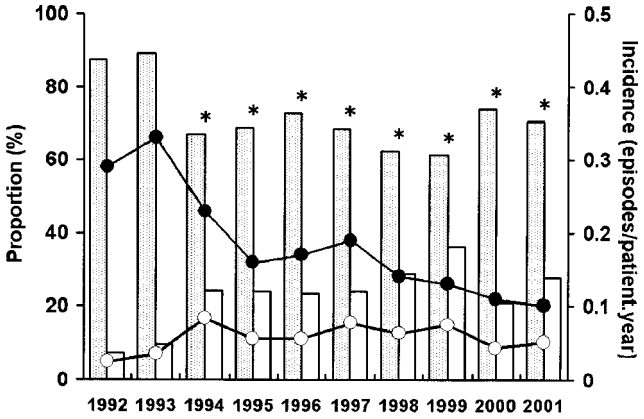

Figure 1 — The proportions and incidences of peritonitis due to a single gram-positive (proportion: shaded bars; incidence: closed circles) and a single gram-negative organism (proportion: white bars; incidence: open circles). Compared with 1992 – 1993, the incidence of peritonitis due to a single gram-positive organism decreased significantly after 1994, whereas that of gram-negative peritonitis increased, resulting in a significant increase in the proportion of gram-negative peritonitis after 1994. *$p < 0.05$ versus 1992 – 1993.

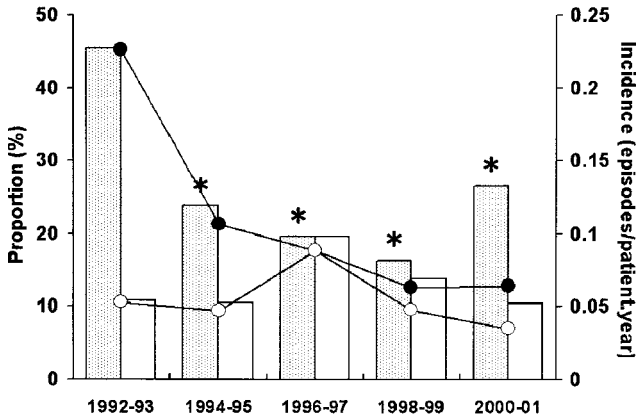

Figure 2 — The proportions and incidences of peritonitis due to coagulase-negative staphylococcus (CoNS) (proportion: shaded bars; incidence: closed circles) and *Staphylococcus aureus* (proportion: white bars; incidence: open circles). The incidence of CoNS-induced peritonitis decreased from 0.226 episodes/patient-year in 1992 – 1993 to 0.064 episodes/patient-year in 2000 – 2001. On the other hand, the incidence of peritonitis due to *S. aureus* remained at a steady level. There was also a significant decrease in the proportion of peritonitis caused by CoNS after 1994 compared with 1992 – 1993. *$p < 0.01$ versus 1992 – 1993.

tis due to a single gram-positive organism was due mainly to a significant decrease in CoNS-induced peritonitis. The incidence of CoNS-induced peritonitis decreased from 0.226 episodes/patient-year in 1992 – 1993 to 0.064 episodes/patient-year in 2000 – 2001. On the other hand, the incidence of peritonitis due to *S. aureus* remained at a steady level. There was also a significant decrease in the proportion of peritonitis caused by CoNS after 1994 compared with 1992 – 1993 ($p < 0.01$) (Figure 2).

When the causative organisms of peritonitis were analyzed according to duration of CAPD before the onset of peritonitis, there was no difference in the incidence of peritonitis between gram-positive and gram-negative organisms (data not shown).

ANTIMICROBIAL SUSCEPTIBILITY OF GRAM-POSITIVE ORGANISMS

Coagulase-Negative Staphylococcus: Of the 279 episodes of peritonitis caused by CoNS, 206 (73.8%) were caused by methicillin-sensitive (MS-) CoNS and 73 (26.2%) by methicillin-resistant (MR-) CoNS. The incidence of peritonitis due to MS-CoNS showed a steady decrease over time (0.184, 0.082, 0.070, 0.042,

and 0.037 episodes/patient-year in 1992 – 1993, 1994 – 1995, 1996 – 1997, 1998 – 1999, and 2000 – 2001, respectively), whereas that of MR-CoNS-induced peritonitis remained at a constant level, resulting in a significant increase in the proportion of peritonitis due to MR-CoNS after 1998 ($p < 0.05$) (Figure 3).

Staphylococcus aureus: Staphylococcus aureus was the etiologic agent in 151 episodes of peritonitis; 35.1% showed resistance to methicillin (MRSA). There was no difference in the incidence of peritonitis due to MSSA and MRSA by calendar year (Figure 4).

Enterococcus: Enterococcus species were responsible for 13 episodes of peritonitis: 6 (46.2%) were caused by *E. faecalis* and 7 (53.8%) by *E. faecium*. All *E. faecalis* showed sensitivity to ampicillin, whereas all *E. faecium* were resistant to ampicillin. Vancomycin-resistant enterococcus was isolated in 1 of 13 episodes (7.7%). There was no significant change in the incidence of peritonitis due to *Enterococcus spp* during the study period (data not shown).

ANTIMICROBIAL SUSCEPTIBILITIES OF GRAM-NEGATIVE ORGANISMS

There was no difference among *E. coli*, *P. aeruginosa*, and other gram-negative organisms in their susceptibility to aminoglycosides, including tobramycin, gentamicin, and amikacin. Although the susceptibilities of *E. coli* and *P. aeruginosa* to quinolone were not different, they were significantly lower than those of other gram-negative organisms ($p < 0.05$) (Table 4). All gram-negative organisms showed sensitivity to imipenem since 1993, when imipenem was introduced for sensitivity testing. There was no significant change in the antimicrobial susceptibility of gram-negative organisms during the study period (data not shown).

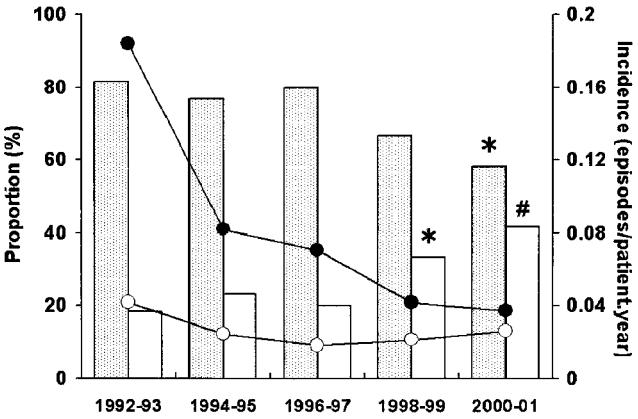

Figure 3 — The proportions and incidences of peritonitis due to methicillin-sensitive coagulase-negative staphylococcus (MS-CoNS) (proportion: shaded bars; incidence: closed circles) and methicillin-resistant (MR-) CoNS (proportion: white bars; incidence: open circles). The incidence of MS-CoNS-induced peritonitis showed a steady decrease over time (from 0.184 episodes/patient-year in 1992 – 1993 to 0.037 episodes/patient-year in 2000 – 2001), whereas that of MR-CoNS-induced peritonitis remained at a constant level, resulting in a significant increase in the proportion of peritonitis due to MR-CoNS after 1998. *$p < 0.05$ versus 1992 – 1993, 1994 – 1995, and 1996 – 1997; #$p < 0.01$ versus 1992 – 1993, 1994 – 1995, and 1996 – 1997.

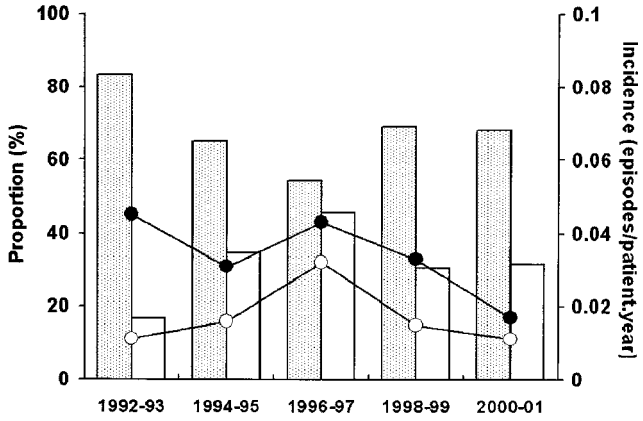

Figure 4 — The proportions and incidences of peritonitis due to methicillin-sensitive *Staphylococcus aureus* (MSSA) (proportion: shaded bars; incidence: closed circles) and methicillin-resistant SA (MRSA) (proportion: white bars; incidence: open circles). There was no difference in the incidences and proportions of peritonitis due to MSSA and MRSA by calendar year.

OUTCOME (TABLE 5)

In 109 (9.8%) of 1108 episodes of peritonitis, the patients were transferred to hemodialysis following removal of the peritoneal catheter. Among those 109 patients, 19 returned to CAPD after complete resolution of peritonitis, 66 remained on hemodialysis, and 24 patients died of peritonitis-associated complications. Catheter removal rates were significantly higher in peritonitis due to a single gram-negative organism (27/163, 16.6%) compared with gram-positive peritonitis (24/498, 4.8%) ($p < 0.005$). Mortality associated with peritonitis was also higher in gram-negative (6/163, 3.7%) compared with gram-positive peritonitis (7/498, 1.4%), but there was no statistical significance.

Gram-Positive Peritonitis: Among episodes due to a single gram-positive organism, catheter removal rates were significantly higher in those due to *S. aureus* (14/151, 9.3%) compared with those due to CoNS (8/279, 2.9%) ($p < 0.01$) and other gram-positive organisms (2/68, 2.9%) ($p < 0.05$). In contrast, there was no statistically significant difference in peritonitis-related mortality between those three groups.

TABLE 4
Antimicrobial Susceptibilities of Gram-Negative Organisms

Organisms	Isolates (*n*)	Susceptibility (%) Tobramycin S	Tobramycin R	Gentamicin S	Gentamicin R	Amikacin S	Amikacin R	Quinolone S	Quinolone R
Escherichia coli	60	91.7	8.3	78.3	21.7	98.3	1.7	90.0	10.0
Pseudomonas aeruginosa	32	84.4	15.6	87.5	12.5	93.8	6.2	90.6	9.4
Other gram negatives	71	88.7	11.3	90.1	9.9	91.5	8.5	100	0[a]

S = susceptible; R = resistant.
[a] $p < 0.05$ versus *E. coli* and *P. aeruginosa*.

TABLE 5
Catheter Removal and Peritonitis-Associated Death According to Causative Organism

Organism	Isolates (*n*)	Removals [*n* (%)]	Deaths [*n* (%)]
Gram positives	498	24 (4.8)	7 (1.4)
Staphylococcus aureus	151	14 (9.3)	4 (2.7)
CoNS	279	8 (2.9)	2 (0.7)
Streptococcus sp	55	1 (1.8)	1 (1.8)
Enterococcus sp	13	1 (7.7)	1 (7.7)
Gram negatives	163	27 (16.6)	6 (3.7)
Pseudomonas aeruginosa	32	14 (43.8)	2 (6.3)
Escherichia coli	60	3 (5.0)	1 (1.7)
Serratia sp	9	3 (33.3)	0 (0.0)
Klebsiella sp	13	3 (23.1)	2 (15.4)
Enterobacter sp	8	1 (12.5)	1 (12.5)
Other gram negative	41	3 (7.3)	0 (0.0)
Multi-organism	13	4 (30.8)	1 (7.6)
Fungi	24	24 (100)	7 (29.2)
Mycobacterium tuberculosis	1	1 (100)	0 (0.0)
Culture negative	409	29 (7.1)	3 (0.7)
Total	1108	109 (9.8)	24 (2.2)

CoNS = coagulase-negative staphylococcus.

When catheter removal rates were compared according to antimicrobial susceptibility in CoNS, they were significantly higher in the MR group (6/73, 8.2%) compared with the MS group (2/206, 1.0%) ($p < 0.01$). In contrast, there was no statistical difference between MRSA (8/98, 8.2%) and MSSA (6/53, 11.3%).

Gram-Negative Peritonitis: Among 163 episodes of peritonitis due to a single gram-negative organism, the peritoneal catheter was removed in 27 episodes (16.6%). Catheter removal rates were significantly higher in peritonitis due to *P. aeruginosa* (14/32, 43.8%) compared with those due to *E. coli* (3/60, 5.0%) ($p < 0.005$) or other gram-negative organisms (10/71, 14.1%) ($p < 0.01$). Mortality associated with *Klebsiella*-induced peritonitis was the highest (2/13, 15.4%) among the gram-negative peritonitis, but there was no significant difference in mortality according to causative organisms.

Fungal and Tuberculous Peritonitis: In all episodes of fungal and the 1 episode of tuberculous peritonitis, the peritoneal catheter was removed. Mortality related to fungal peritonitis was significantly higher (7/24, 29.2%) compared with that associated with gram-positive (7/498, 1.4%) ($p < 0.001$), gram-negative (6/163, 3.7%) ($p < 0.001$), and culture-negative peritonitis (3/409, 0.7%) ($p < 0.001$).

Culture-Negative Peritonitis: Among the 409 episodes of culture-negative peritonitis, 307 episodes (75.1%) responded to the empirical antibiotics, cefazolin and tobramycin, and 73 episodes (17.8%) to the second-line drugs, vancomycin and amikacin. The peritoneal catheter was removed in 29 episodes (7.1%) of culture-negative peritonitis because of no clinical improvement.

DISCUSSION

To the best of our knowledge, this is the first study investigating changes in the causative organisms of peritonitis and their antimicrobial susceptibilities in more than 1000 CAPD patients, and during 10 years at a single center.

In the 1990s, the incidence of peritonitis decreased significantly, to 1 episode/24 patient-months. This change was due to improvement in connect systems, development of new dialysis solutions, improvements in living environments, and education of patients (5–8). In the present study, we also found a decreased incidence of peritonitis from 1992 to 2001, in which the incidence was 0.23 episodes/patient-year, being less than 50% of the 0.49 episodes/patient-year in 1992. Considering the fact that the double-bag system was introduced in the Severance Hospital in the early 1990s, and about 35% of our patients were on the double-bag system in 1992 and more than 95% after 1995, the decrease in the incidence of peritonitis due to a single gram-positive organism, especially CoNS, between 1992 and 1994 might have resulted from the new connect system. However, even after extensive usage of the double-bag system, the incidence of peritonitis decreased steadily.

It has been shown that the incidence of peritonitis differs according to patient demographics, such as race (21–23) and age (24,25), mode of PD (CAPD vs automated PD) (26), and composition of dialysis solutions (27). In the present study, all the subjects were Korean, and there was a small increase in the proportion of diabetics and the age of patients after 1995. In addition, all the patients included in this study were on CAPD and used conventional lactate-based solution. Therefore, we are inclined to believe that the specially trained nurses in our PD unit, who participated in training new CAPD patients and in educating patients who visited our PD unit due to peritonitis, and the patient education program, which has been in operation since 1995, contributed to this decrease. Our education program for new CAPD patients consists of 1 hour for 2 days. On the first day, patients learn the basic physiology of PD and how to exchange dialysate; on the second day, they learn PD complications and how to deal with these problems.

The use of intraperitoneal antibiotics is a standard treatment of peritonitis; initial empirical antibiotics are determined by the major organisms responsible for peritonitis. Based on differences in the epidemiology of the causative organisms and in their antimicrobial susceptibilities, many investigators (28,29) suggest that individual centers should continuously monitor the epidemiology of CAPD peritonitis, and that the management of peritonitis should be adapted to the local situation in a "center tailored" treatment protocol. Nevertheless, only a few studies have attempted to examine the epidemiology of the causative organisms and their antimicrobial susceptibilities (28,30–32), and there has been only one report at a single center on changes in antimicrobial susceptibility according to each organism (13).

Among gram-positive organisms, we found that the incidence and the proportion of peritonitis due to MRSA had increased during 1992 and 1997; however, they deceased to levels similar to 1992 – 1993. On the other hand, the proportion of peritonitis due to MR-CoNS, which is the most common causative organism of CAPD peritonitis, has been on the rise steadily since 1992. An increase in MR *S. epidermidis*, which is often resistant to multiple antibiotics, from blood isolates has been reported (33). Zelenitsky *et al.* (13) have also observed that, among *S. epidermidis* peritonitis, resistance to methicillin increased from 18.9% in 1991 – 1992 to 73.9% in 1997 – 1998. In addition, some authors recommend a switch from cefazolin or cephalothin to vancomycin because treatment of patients with an antibiotic showing very high resistance was not warranted (31,32). In view of the significant changes in the antimicrobial susceptibility of CoNS observed in our present study, we suggest that the use of first-generation cephalosporin as the initial empirical antibiotic, which has been recommended by the ISPD (18), should be limited.

There have been many studies on the effect of *S. aureus* prophylaxis on the prevention of peritonitis, but the results are controversial (34–36). In the present study, we could not evaluate the effect of *S. aureus* prophylaxis in our patients because it has never been performed at our institute.

Similar to earlier studies (5,11–13,28,37), the proportion of peritonitis due to *E. coli* and *P. aeruginosa* among gram-negative organisms was found to be high. In the present study, susceptibility to aminoglycosides, which are used as the initial empirical antibiotic, was not statistically different among *E. coli*, *P. aeruginosa*, and other gram-negative organisms. However, *E. coli* and *P. aeruginosa* showed relatively high resistance to gentamicin and tobramycin respectively. Millikin *et al.* (30) also found that only 48% of gram-negative peritonitis responded to aminoglycoside monotherapy, whereas 75% responded to combination regimens. This relatively high resistance to aminoglycoside led us to consider new center-based guidelines for the treatment of peritonitis. In this study, we could not evaluate susceptibility to ceftazidime, an antibiotic recommended as an initial empirical drug by the ISPD (18), because its susceptibility was routinely tested only after mid-1990s, and the National Health Insurance Corporation in Korea does not permit ceftazidime as an empirical drug.

When clinical symptoms and signs do not improve with appropriate intraperitoneal antibiotics, the catheter should be removed and systemic antibiotics administrated for at least 1 week. Catheter removal rates were significantly lower in peritonitis due to a single gram-positive organism than in those due to a single gram-negative organism or fungus, a finding consistent with previous studies (12,16,17). However, among gram-positive organisms, catheter removal rates in peritonitis due to MR-CoNS, which have been increasing recently, were significantly higher than MS-CoNS, thus we expect a gradual increase in catheter removal rates in the future.

We experienced catheter removal rates similar to those of Troidle *et al.* (16) in peritonitis due to a single gram-negative organism. Peritonitis due to *P. aeruginosa* usually accompanies more severe symptoms and does not respond well to antibiotics, resulting in high catheter removal rates: up to 50% – 100% (30,38–40). However, in the present study, we found a relatively low catheter removal rate of 43.8%, due probably to early and prolonged use of newly developed anti-pseudomonas antibiotics, combination regimens, and a well-designed patient education program. Taber *et al.* (41) also observed that, of 7 patients with peritonitis caused by *Pseudomonas sp* (*aeruginosa*, *fluorescens*, *stutszeri*, and *maltophilia*), 5 patients

were cured with the combination of ceftazidime and ciprofloxacin, suggesting that a combination regimen could result in a better response rate in pseudomonas peritonitis.

It should be noted that we had a higher proportion of culture-negative peritonitis in this study than the generally accepted rate of 10% – 20% (7,13,37). Even though it is difficult to explain the high incidence in a retrospective study, it might have been due partly to the use of intraperitoneal antibiotics prior to visits to our PD unit. All the patients were taught to bring the first cloudy dialysate, but compliance was not good enough. This high proportion of culture-negative peritonitis could lead to misinterpretation of the results. Therefore, to minimize this confounding effect, we analyzed not only the incidence but also the proportion of causative organisms after excluding culture-negative peritonitis. Use of antibiotic-removing or -neutralizing resin in these cases could be an alternative to lower the rate of culture-negative peritonitis.

In conclusion, the incidence of peritonitis in 2001 is less than a half that of 1992, concomitant with an increase in the proportion of peritonitis due to a single gram-negative organism and MR-CoNS. Consequently, it is necessary to prepare new center-based treatment guidelines for CAPD peritonitis.

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