

# Peritoneal dialysis - related peritonitis - analysis of the local microbiology and sensitivity pattern of causative organisms

Maksić Đ<sup>1</sup>, Mirović V<sup>2</sup>, Tomanović B<sup>2</sup>, Nonković Z<sup>2</sup>, Aleksić S<sup>1</sup>, Kovacević Z<sup>1</sup>

Clinic of Nephrology<sup>1</sup>, Institute for microbiology<sup>2</sup>, Military Medical Academy, Belgrade

## Introduction

Although incidence rates of CAPD peritonitis have decreased substantially with the introduction of the flush-before fill double-bag principle, and the emergence of improved connection system, peritonitis remains an Achilles tendon for peritoneal dialysis (PD). A variety of microorganisms may cause PD peritonitis. Gram-positive organisms, particularly *Staphylococcus aureus* and *S. epidermidis*, have been the most frequent pathogens. However, in patients utilizing the disconnect systems, the relative incidence of gram negative infection has increased. Mortality rate directly related to peritonitis is low, but peritonitis episodes cause psychosocial problems and can also damage the peritoneal membrane (1, 2).

Aim of the study was to assess the rate of peritonitis, causative organisms and antibiotic susceptibility in our CAPD patients.

## Materials and methods

In 98 CAPD patients aged  $50.46 \pm 18.18$  years in average, 201 episodes of peritonitis were diagnosed within the period 1998-2002, that is, one episode per 23.9 months of treatment. Average dialysis period was  $32.58 \pm 22.18$  months. The most frequently used systems were A.N.D.Y. (70% of patients), that is, Stay Safe, Stay Safe Balance and Gambrosol bio trio (30% of patients). Dialysis effluent samples from the drainage bag were taken under sterile conditions and 5 ml was cultured in both aerobic and anaerobic hemoculture bottles, and the remained 20 ml was used for direct Gram staining. Automatic continuous bacterial and fungal growth was monitored by the Bac T/Alert Organon Techniques. Owing to rapid isolation and identification of the most causative agents of CAPD peritonitis together with the rapid blood culture techniques, the highest culture percentage (75%) was positive within the first 24 and for the remained ones within less than the following 72 hours. Patients were particularly informed about importance of the effluent taking from the first cloudy bag. It was repeated only when number of elements at cytologic examination was not reduced or even increased during the first three days. Findings of causative agents isolation and their sensitivity specifications enabled us analysis of the local peritonitis epidemiology which is condition sine qua non for the adequate strategy in its treatment.

## Results

Growth of the Gram-positive bacteria was observed in 149 (75.12%), of Gram-negative in 24 (11.94%) and of fungi (*Candida* and *Aspergillus* genus) in 8 (3.79%) cultures of the dialysis effluent. Culture was sterile in 18 patients (8.95%), but TBC peritonitis was confirmed in 2 patients after laparoscopic catheter removal and peritoneal biopsy.

**Figure 1. Incidence of isolated Gram-positive microorganisms in patients on peritoneal dialysis (Military Medical Academy, 1998-2002)**

	1998	1999	2000	2001	2002	Total
1. CNS	15	20	21	13	12	81
2. <i>S. aureus</i>	3	3	2	3	3	14
3. <i>Enterococcus. sp</i>	8	5	3	3	3	22
4. <i>Streptococcus vir.</i>	2	4	3	1	1	11
5. <i>Corinemorf bacilli</i>	4	2	3	2	2	13
6. <i>Streptococcus pn.</i>	1	-	-	1	-	2
7. <i>Bacillus sp.</i>	1	2	2	1	-	6
Total	34	36	34	24	21	149

The most common isolated Gram-positive bacteria were CNS, *Enterococcus* species, *Staphylococcus aureus*, *Corinemorf bacilli*, *Streptococcus viridans* and *Bacillus* species, and Gram-negative were *Klebsiella pneumoniae*, *Pseudomonas* species, *Citrobacter*, *E. Colli*, *Proteus mirabilis* and *vulgaris*, *Acinetobacter* (Figures 1 and 2). *Candida albicans* was isolated in 6 cultures and *Candida parapsilosis* as well as *Aspergillus flavus* in 1 each. Isolated strains of CNS were 100% sensitive to Vancomycin, 77.3% of strains to Rifampin, 73.1% to Gentamycin and 67.1% to erythromycin. To fucidinic acid, trimethoprim/sulfamethoxazole, ciprofloxacin and methicillin-cloxacillin 65.5%, 60.2%, 56.8% and 34.8% of CNS strain were sensitive, respectively. Sensitivity of isolated *S. aureus* strains to Vancomycin was 100%, to Fucidinic acid 93.3%, to trimethoprim/sulfamethoxazole 90.9%, to clindamycin and erythromycin 63.6% and to rifampin 60%. 53.8% of isolated *S. aureus* strains were sensitive to methicillin-cloxacillin. Isolated enterococcus strains were 100% sensitive to Vancomycin, 83.3% to ampicillin, 72.7% to erythromycin, 40% to gentamicin and 26.9% to ciprofloxacin. Isolated enterobacteriaceae strains were in 100% cases sensitive to Imipenem, in 77.8% to amikacin, in 67.8% to ciprofloxacin, in 60% to trimethoprim/sulfamethoxazole, in 50% to ceftazidim and only in 3.4% to ampicillin.

Correspondence to:

Maksić Djoko, Crnotravska 17 VMA, Belgrade, Serbia and Montenegro, tel: 381 112 661 122  
 Fax: 381 11 666 164, e-mail: djmaksic@eunet.YU

**Figure 2. Incidence of isolated Gram-negative microorganisms in patients on peritoneal dialysis (Military Medical Academy, 1998-2002)**

	1998	1999	2000	2001	2002	Total
1. Klebsiela pn.	2	1	1	1	2	7
2. Citrobacter sp.	1	2	-	-	1	4
3. E.colli	-	1	1	1	-	3
4. Pseudomonas p.	2	1	1	2	-	6
5. Proteus vulgaris	1	-	1	1	-	3
6. Acinetobacter lw.	1	-	-	-	-	1
Total	7	5	4	5	3	24

According to the local epidemiological situation our previous initial empirical therapy was Vancomycin-Cephtazidine/Netilmicin in dependence of the residual renal function presence. Owing to administration protocol of this antibiotic combination followed by the prolonged antibiotic therapy after obtaining isolated causative microorganisms, peritonitis was cured in 88.1% of episodes. In only 10% of bacterial peritonitis episodes peritoneal catheter had to be removed, but in most cases it was reinserted after 14-21 days. Mortality rate for our patients on CAPD during peritonitis episodes was 0.9% mostly for reasons not related to the infection.

**Discussion**

Owing to appropriate selection and good patient training, usage of the double-bag dissonect system as well as to prophylactic administration of antibiotics, incidence of CAPD peritonitis was in our patients 1 episode per 23.9 months of therapy. The correct microbiological culture of PD samples is of utmost importance to establish the etiological agent and appropriate antibiotic therapy. The speed with which bacteriological diagnosis can be established is very important. Rapid blood culture techniques (e.g. Bac T/Alert) may further speed up isolation and identification (3). The most common isolated causative microorganisms of CAPD peritonitis in our patients were Gram-positive bacteria, which is in accordance with other authors' findings. CNS was responsible for 81 peritonitis episodes, representing 40.29% of all its episodes. The other authors' findings present CNS as the causative agent of CAPD peritonitis in 15% to 43% of cases (4-6). Methicillin-resistant were 65.29% of isolated CNS strains, which is comparable with other authors' results ranging from 39% to 80% of cases (1,6). In contrast to other authors' results isolated CNS strains did not show Vancomycin-resistance in our patients. Namely, the worldwide increasing number of CAPD peritonitis is caused by Vancomycin-resistant CNS strains presenting a great problem with regard to antibiotic selection and possible satisfactory treatment as well as development of numerous complications during the treatment period. Readministered Vancomycin in empirical therapy of CAPD peritonitis, very often in suboptimal doses, resulted in development of Vancomycin-resistant enterococci, which is currently a great problem in some clinical centers. Some centres report Vancomycin-resistant enterococcal infec-

tions in up to 20% of cases as well as documented cases of Vancomycin-resistant CAPD enterococcal peritonitis (7). Isolated enterococcal strains were in our patients Vancomycin-sensitive in 100% of cases and ampicillin and erythromycin-sensitive was found in 83.3% and 72.7% of isolated strains.

Isolated Staph. Aureus strains showed methicillin-resistance in 46.2% of cases representing considerably higher percentage in comparison with results other authors (1, 4, 6). All this indirectly suggests considerable percentage of CAPD peritonitis episodes caused by methicillin-resistant Gram-positive bacteria (20% of all peritonitis episodes), which is of great importance having in mind local epidemiological situation including antibiotic selection in empirical therapy. Isolated Staph. Aureus strains were not Vancomycin-resistant in our patients and more than 90% of strains were in vitro both fucidinic acid and trimethoprim/sulfamethoxazole-sensitive. Some authors have described cases with Staph. Aureus Vancomycin-intermediately sensitive (VISA) infections (4). Isolated enterobacteriaceae strains were in vitro sensitive to only one antibiotic (Imipenem). Sensitivity to Cefazidime, cephalosporin of the 3<sup>th</sup> generation used for initial empirical therapy of peritonitis in patients with residual diuresis more than 100 ml/24 hours, was only 50%. Poor initial response to the given initial empirical therapy (Cefazolin + Cefazidime /aminoglycoside) in the case of enterobacteriaceae isolation implicated necessity of Cefazolin therapy discontinuation and inclusion of another antibiotic, additional to ceftazidime (aminoglycoside or ciprofloxacin, less frequently trimethoprim/sulfamethoxazole). Poor response to combined antibiotic therapy with presence of exit-site infection is an indication for peritoneal catheter removal and for continuation of parenteral antibiotic therapy (1,5). Percentage of CAPD peritonitis with sterile cultures was less than 9% being considerably lower in comparison with other authors' findings reporting peritonitis with sterile cultures in up to 20% of cases (5). The mentioned differences can be explained by common and numerous technical and clinical reasons also including mycobacterial and rare fungal infections.

**Conclusions**

The most common causative microorganisms of CAPD peritonitis in our patients are still Gram-positive bacteria. Significant incidence of CNS suggests necessity for better education of our patients and introduction of more reliable and safer double-bag disconnect systems in larger number of patients. High percentage of methicillin-resistant CNS and Staph. Aureus strains, regardless of the 100% of isolated Vancomycin-sensitive strains as well as of absence of Vancomycin-resistant enterococci, obliges us to strictly obey recommendations of the empirical antibiotic therapy. Local epidemiologic situation should be monitored and registers for causative agents and their antibiotic sensitivity should be introduced.

---

**References**

1. Fried L, Piraino B. Peritonitis. In: Gokal R, Khanna R, Krediet R, Nolph K, editors. Textbook of peritoneal dialysis. Dordrecht, Boston, London: Kluwer Academic Publishers, 1999:545-65.
2. Prasad N, Gupta A, Sharma K.R, Prasad K.N, Gulati S, Sharma A.P. The spectrum of bacterial peritonitis in CAPD patients in a developing country: Is it different? *Perit Dial Int* 2003;23 (4): 400-3.
3. Shetty H, Gokal R. Treatment of infections in peritoneal dialysis. In: Ronco C, Dell'Aquila R, Rodighiero P.M, eds. *Peritoneal dialysis today*. Basel: Karger AG,2003:187-95.
4. Teitelbaum I. Vancomycin for the initial therapy of peritonitis: Dont throw out the baby with the bathwater. *Perit Dial Int* 2001;21(3): 235-39.
5. Keane W.F, Bailie G.R. Boeschoten E, Gokal R, Golper T.A, Holmes C.J. et al. Adult peritoneal dialysis related-peritonitis treatment recommendations: 2000 Update. *Perit Dial Int* 2000; 20(4):396-412.
6. Herwaldt L.A, Boyken L.D, Coffman S, Hochstetler L, Flanigan M.J. Sources of Staphylococcus Aureus for patients on Continuous Ambulatory Peritoneal Dialysis. *Perit Dial Int* 2003; 23(3):237-42.
7. Van Biesen V, Veys N, Vanholder R, Lameire N. Peritoneal dialysis-related peritonitis: the art of rope-dancing. *Nephrol Dial Transplant* 2002;17(11):1878-83.