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Research

Peritoneal Dialysis-related Peritonitis: Microbiological Profile and Outcome

Periton Diyalizi İlişkili Peritonit: Mikrobiyolojik Etkenler ve Klinik Sonlanım

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ABSTRACT

Objective: Peritonitis is a major complication of peritoneal dialysis (PD) and leads to significant mortality and technical failure. Understanding local peritonitis rates and microbiologic profiles are important for the prevention and appropriate management of PD-related peritonitis. We investigated the incidence rate, causative agents, and outcomes of PD-related peritonitis episodes.

Methods: This retrospective study enrolled all patients who were receiving PD and have been treated for PD-related peritonitis between February 2005 and November 2021 in our PD unit. Data of the patients included demographic characteristics, causes of primary renal disease, microbiology, and outcomes (resolution, catheter loss, and death) of peritonitis episodes.

Results: During the study period, 143 PD-related peritonitis episodes were identified in 69 patients. The peritonitis rate was 0.56 episodes per patient-year. Overall, 62.9% of the episodes were due to Gram-positive organisms, 32.1% were due to Gram-negative organisms, 3.4% were culture negative and 1.3% were candida. Coagulase-negative *staphylococci* were isolated in half of the Gram-positive episodes. *Acinetobacter* and *Pseudomonas* were the most frequently observed microorganisms among Gram-negative episodes. Overall, 81.1% of cases improved completely with medical treatment. The PD catheter was removed in 27 (18.8%) patients, and two patients died from sepsis. Gram-negative organisms resulted in a significantly higher rate of catheter removals and a lower rate of resolution than Gram-positive organisms ($p<0.001$).

Conclusion: Reducing the incidence of PD-related peritonitis could be possible by knowledge of prevalent microbial agents in each center, adjusting empirical treatment accordingly, and taking the necessary measures to prevent peritonitis attacks.

Keywords: Peritoneal dialysis, peritonitis, microbiology, outcome

ÖZ

Amaç: Peritonit, periton diyalizinin (PD) önemli bir komplikasyonudur, teknik yetersizliğe ve morbiditeye yol açabilir. Lokal peritonit oranlarını ve mikrobiyolojik etkenleri anlamak PD ile ilişkili enfeksiyonların önlenmesi ve uygun yönetimi için önemlidir. Bu çalışmada, PD ilişkili peritonitlerin sıklığının, etken mikroorganizmaların ve klinik sonlanımlarının belirlenmesi amaçlanmıştır.

Gereç ve Yöntem: Hastanemiz PD ünitesinde Şubat 2005 ve Kasım 2021 tarihleri arasında PD ile ilişkili peritonit tanısıyla tedavi edilen hastalar çalışmaya alındı. Hastaların demografik verileri, primer böbrek hastalığı nedenleri, peritonit etkenleri ve atakların klinik sonuçları (düzelme, kateter kaybı ve ölüm) kaydedildi.

Bulgular: Çalışma sürecinde, PD uygulayan 69 hastada 143 peritonit atağı saptandı. Peritonit atak sıklığı 0,56 atak/hasta yılı idi. Atakların %62,9'unda Gram-pozitif etkenler, %32,1'inde Gram-negatif etkenler, %1,3'ünde mantarlar saptanırken, %3,4'ünde kültür negatifti. Gram-pozitif atakların yarısında koagülaz negatif *stafilokoklar* izole edildi. En sık saptanan Gram-negatif mikroorganizmalar *Pseudomonas* ve enterokoktu. Tıbbi tedavi ile olguların %81,1'i tam düzeldi. Yirmi yedi (%18,8) hastada PD kateteri çıkarılmak zorunda kalındı ve iki hasta sepsis nedeniyle hayatını kaybetti. Gram-pozitif etkenlerle karşılaştırıldığında; Gram-negatif etkenlere bağlı peritonitlerde iyileşme oranının düşük ve PD kateter çıkarılma oranının daha fazla olduğu görüldü ($p<0,001$).

Sonuç: PD ilişkili peritonit insidansının azaltılması, her merkezin kendi etken mikroorganizma profilini bilmesi, ampirik tedavi seçenekleri belirlemesi ve peritonit ataklarını önlemek için gerekli tedbirleri alması ile mümkün olabilir.

Anahtar Kelimeler: Periton diyalizi, peritonit, mikrobiyoloji, sonlanım

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INTRODUCTION

Peritoneal dialysis (PD) is one of two principal modalities of renal replacement therapy and an alternative to hemodialysis. Despite the advances in technology and antibiotic therapy, PD-related infections, including peritonitis, tunnel infections, and exit-site infections, remain common and serious complications of PD (1). Peritonitis is associated with significant morbidity, structural and functional alterations of the peritoneal membrane, transient loss of ultrafiltration, eventually permanent membrane damage, catheter loss, transfer to hemodialysis, and occasionally death (2-5). Therefore, knowledge of the causative agent, course, and predisposing factors of peritonitis is important for the appropriate management and prevention of PD-related peritonitis. We determined the incidence rate, microbiological characteristics, and outcomes of PD-related peritonitis.

METHODS

This single-center study was conducted through retrospective examination of all patients who were treated for PD-related peritonitis in our PD unit between February 2005 and December 2021. Standard Tenckhoff catheter was placed in all patients with PD. All episodes of PD-related peritonitis were reviewed. Peritonitis was diagnosed if at least two of the following criteria were present: (a) Presence of symptoms and signs related to peritonitis, i.e. a cloudy peritoneal effluent or abdominal pain, (b) peritoneal effluent white blood cell count higher than 100/μL, with at least 50% polymorphonuclear cells, and (c) positive culture of peritoneal effluent. The exclusion criteria was incomplete clinical data. Empirical antibiotic therapy was initiated after appropriate microbiological specimens have been obtained. First, all episodes were treated with ciprofloxacin and intraperitoneal vancomycin, based on the center-specific treatment protocol, unless the patient had features of systemic sepsis. Antibiotic therapy was adjusted as soon as the culture results were obtained. The duration of antibiotic therapy was 14-21 days based on the causative organism.

Demographic and clinical characteristics for all patients, including age, sex, the underlying cause of end-stage renal disease (ESRD), PD modality (continuous ambulatory PD or automated PD), duration of PD, episodes, etiology, and outcomes (resolution, catheter removal, and death) of peritonitis, and presence of concomitant tunnel or exit site infection were recorded. The resolution was defined as the disappearance of signs and symptoms within 96 h after the beginning of antibiotic therapy and a negative peritoneal fluid culture at least 28 days after treatment completion. Death related to peritonitis was defined as the death of the patient with active peritonitis or admitted with peritonitis or death within 30 days of a peritonitis episode. Catheter removal was indicated for refractory or relapsing peritonitis and peritonitis of fungal etiology. Peritonitis rate was calculated as the number of peritonitis episodes per number of patients-years at risk. The time at risk of peritonitis was counted from the first day of training till the occurrence of peritonitis.

This study was approved by the University of Health Sciences Turkey, Hamidiye Clinical Research Ethics Committee (decision no: 5/53, date: 05.02.2021) and adhered to the principles of the Declaration of Helsinki. Patient consent was not obtained due to the retrospective design of the study.

Statistical Analysis

Study results were expressed as numbers and percentages for categorical variables, and means ± standard deviations or data ranges for continuous variables. Variables were compared using the chi-square test. P-values of ≤0.05 were thought to be significant. Data were analyzed using SPSS Statistics version 24 for Windows (IBM, New York, U.S.).

RESULTS

During the study period, 69 (27.9%) of 247 chronic patients with PD developed 143 episodes of PD-related peritonitis over 3,028 patient months, with an overall peritonitis rate of 0.56 episodes/patient year. The demographic data of the patients with PD-related peritonitis are shown in Table 1. Thirty five (50.8%) were female, and 49 (71%) received continuous ambulatory PD. ESRD was most commonly caused by hypertension (40.5%) and diabetic nephropathy (27.5%).

Among the patients with PD-related peritonitis, 35 (50.7%) experienced one episode, 14 (20.2%) had two and the rest of the patients (28.9%) had ≥3 episodes. None of the patients had polymicrobial peritonitis. The distribution of organisms is shown in Figure 1. Gram-positive organisms were identified in 90 (62.9%) of peritonitis episodes. Among Gram-positive organisms, coagulase-negative *staphylococci* (CNS) was the most common Gram-positive species, accounting for 30.7% of total episodes and 48.8% of Gram-positive episodes. Gram-negative organisms were isolated in 32.1% of episodes. Among Gram-negative organisms, *Acinetobacter* and *Pseudomonas* contributed equally, followed by *Escherichia coli* and *enterobacter*. Fungal infections were observed in 1.3% of episodes and

culture-negative peritonitis was seen in 3.4% of episodes.

Organism-specific outcomes are shown in Table 2. Overall, Gram-positive infections were characterized by greater resolution with therapy and lesser need for catheter removal than Gram-negative organisms (88.8% vs 58.7%, and 10% vs 39%, p≤0.001, respectively). Among Gram-positive organisms, methicillin-resistant *Staphylococcus aureus* (MRSA) resulted in the highest catheter removal rate (23.8%). *Klebsiella* infections had the worst outcome with a 75% catheter removal rate and 25% of mortality. Fungal infections almost always resulted in catheter removal. The overall catheter removal rate was 18.8%. Two episodes resulted in death, which is caused by MRSA and *Klebsiella*.

DISCUSSION

This study describes the microbiological profiles and outcomes of PD-related peritonitis. Our data showed that Gram-positive organisms are the main etiological agents of peritonitis. Moreover, the results demonstrated that gram-negative organisms are associated with a lower resolution rate and a higher need for catheter removal, and candida infections always resulted in catheter loss.

There is a substantial variation in the incidence of PD-related peritonitis reported by different centers and countries, ranging from 0.06 to 1.66 episodes/patient-year (6). This probably result from different practices in the use of prophylactic antibiotics, in the training of PD staff, and varieties in guidelines (7). In our center, the overall incidence rate of PD-related peritonitis was 0.56 per patient-year at risk, which is higher than the International Society of Peritoneal Dialysis (ISPD) limit of 0.5 episodes per patient-year (8).

The present results showed that Gram-positive peritonitis rates exceed Gram-negative rates, similar to the previous studies in which Gram-positive bacteria accounted for approximately two-thirds of the peritonitis episodes (9-

Table 1. Patients demographics

Characteristics	Patients (n=69)
Male (%)	34 (49.2)
Age (years)	56.3±16.2
PD duration (months)	43.8±29.7 (3-149)
PD type	
CAPD	49 (71)
APD	12 (17.3)
CAPD/APD	8 (11.5)
Primary renal disease	
Hypertension	28 (40.5)
Polycystic kidney disease	3 (4.3)
Diabetic nephropathy	19 (27.5)
VUR	3 (4.3)
Glomerulonephritis	4 (5.7)
Unknown	12 (17.3)

Data are shown as mean ± standard deviation, number, and percentages.
APD: Automated peritoneal dialysis, CAPD: Continuous ambulatory peritoneal dialysis, VUR: Vesicoureteric reflux

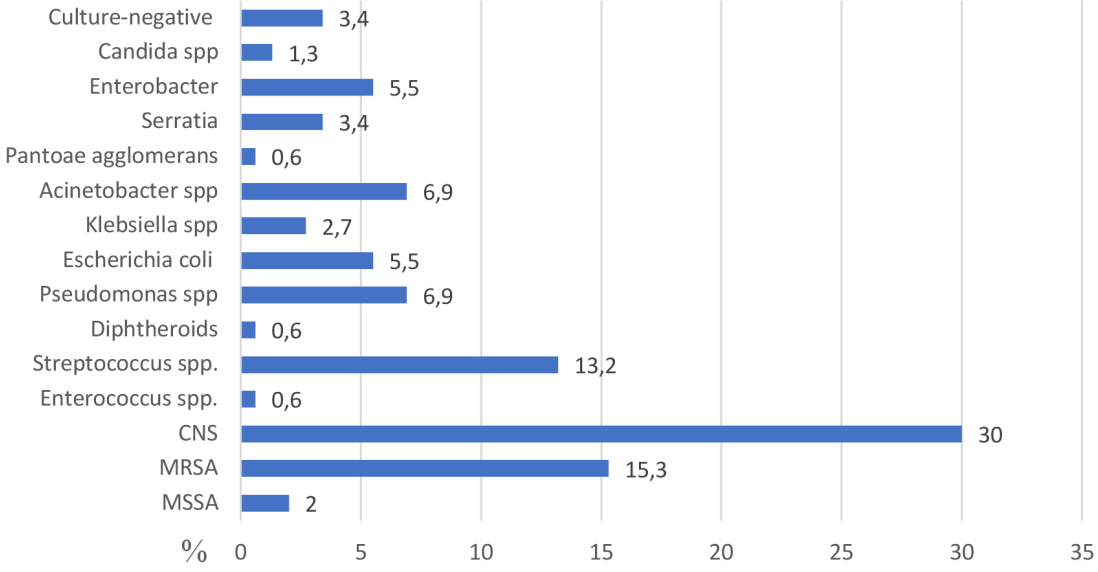

Figure 1. Microbiology of peritonitis
CNS: Coagulase-negative *staphylococci*, MRSA: Methicillin-resistant *Staphylococcus aureus*, MSSA: Methicillin-sensitive *Staphylococcus aureus*

Table 2. Microbiology and outcome of peritonitis episodes

Organism	Episode (n=143)	Resolution (n=112)	Catheter removal (n=29)	Death (n=2)
Gram-positive	90 (62.9)	80 (88.8)	9 (10)	1 (1.1)
Coagulase-negative *staphylococci*	44 (30)	40 (91)	4 (9)	-
Staphylococcus aureus excluding MRSA	3 (2)	-	-	-
MRSA	22 (15.3)	16 (72.7)	5 (22.7)	1 (4.5)
Streptococcus viridans	19 (13.2)	-	-	-
Enterococcus	1 (0.6)	-	-	-
Diphtheroids (Corynebacterium)	1 (0.6)	-	-	-
Gram-negative	46 (32.1)	27 (58.7)	18 (39.1)	1 (2.1)
Escherichia coli	8 (5.5)	7 (87.5)	1 (12.5)	-
Pseudomonas	10 (6.9)	7 (0)	3 (30)	-
Klebsiella	4 (2.7)	-	3 (75)	1 (25)
Enterobacter	8 (5.5)	6 (75)	2 (25)	-
Serratia	5 (3.4)	2 (40)	3 (60)	-
Acinetobacter	10 (6.9)	4 (40)	6 (60)	-
Pantoea agglomerans	1 (0.6)	-	-	-
Fungal (candida)	2 (1.3)	-	2 (100)	-
Culture-negative	5 (3.4)	5 (100)	-	-

Data are expressed as numbers and percentages. MRSA: Methicillin-resistant *Staphylococcus aureus*

11). Among gram-positive peritonitis, CNS was the most common organism isolated in the current study, in line with the literature (12-14). Moreover, *Pseudomonas* and *Acinetobacter* were the most commonly isolated organisms among Gram-negative peritonitis episodes in our study, in contrast with previous studies in which *Escherichia coli* was the most common causative agent (13,15,16). Interestingly, 6 patients developed *Acinetobacter* infection at the same time in our facility and PD catheter was removed in all of them. *Acinetobacter* is rarely reported in association with PD-related peritonitis but it results in serious infection and increases the possibility of drop-out or mortality. In a multicenter study conducted in Australia (17), 253 (2.3%) of 11.122 peritonitis episodes were developed due to Acinetobacter species. One hundred thirty one (74%) out of 176 patients who developed a single episode of *Acinetobacter* peritonitis recovered completely with antibiotic therapy. In contrast to our results, Htay et al. (17) reported that the rates of withdrawal of PD catheter and conversion to hemodialysis were lower with *Acinetobacter* peritonitis than with *Pseudomonas* peritonitis. *Acinetobacter* can be isolated from skin, respiratory tract, and aqueous sources including river waters, humidifiers, and water baths used to warm peritoneal dialysate before administration. The most common causes of *Acinetobacter* peritonitis in patients with PD are a break in exchange sterility, and exit site infection/tunnel infection. None of the participants in our cohort had exit site infection or tunnel infection. We suggested that the development of *Acinetobacter* peritonitis results from the hygiene breaks and contaminated medical equipment. Appropriate measures, such as education of patients, healthcare providers, and caregivers on good hygiene were taken. Additionally, healthcare providers paid attention to infection control practices, including rigorous cleaning of the shared medical equipment and patient rooms to reduce the spread of *Acinetobacter*.

The culture negativity was 3.6% in our study, which is lower than the recommended range by ISPD (8) that should not be more than 20%. Culture negativity may be a result of technical problems with the dialysate cultures, recent antibiotic use, and infection by fastidious organisms. In our center, PD staff takes PD fluid samples for culture in all patients with suspected peritonitis in adherence to international recommendations on diagnostic methods.

Severe and prolonged peritonitis episodes are a major cause of patients discontinuing PD and switching to hemodialysis. Therefore, early and appropriate treatment of peritonitis is important for rapid resolution of inflammation,

preservation of peritoneal membrane function, and patient survival. Our study showed an overall primary cure rate of 81.1%. The catheter was removed in 18.8%, a rate that was similar to previous reports in which the catheter removal rate ranged between 9.8 and 20.4% (12-14,16,18). The closeness of catheter removal rate to the highest level in literature might be explained by a higher rate of Gram-negative peritonitis attacks in our data (32.1%) as numerous studies have reported that Gram-negative peritonitis was associated with a higher rate of antimicrobial resistance, catheter loss, shift of PD to hemodialysis, and death (13,19,20). CNS was accounted for almost half of all Gram-positive episodes. Approximately, 9% of catheters were removed for CNS peritonitis supporting the continued use of empiric vancomycin for Gram-positive cover to control peritonitis attacks. As known, morbidity, and mortality are higher in patients with fungal peritonitis (21). The number of patients with fungal peritonitis in the current study was small but both were switched to hemodialysis.

Peritonitis is rarely associated with a mortal outcome but it is a contributing factor for mortality in 16% of patients with PD related peritonitis (22,23). Two patients died due to *Klebsiella* and MRSA peritonitis septicemia in our cohort.

As we found that the peritonitis rate was higher than the recommended range, we must determine the root cause of each episode, adjust empirical treatments accordingly and take the necessary measures to prevent the peritonitis attacks. Given the most common cause of PD-related peritonitis is Gram-positive microorganism, which is a normal flora of the skin, patient re-education about sterility rules and fluid exchange procedures may prevent peritonitis attacks. Further actions, including developing a home visit protocol to observe patients' home environment are also important in achieving good PD outcomes.

This study has several limitations. First, it has all problems associated with retrospective studies. Second, data of patients with PD without peritonitis were not collected. Therefore, the risk factors associated with peritonitis were not determined. Finally, some results cannot be extrapolated to other centers as the study was conducted at a single center.

CONCLUSION

This study offers insights into the etiology and outcomes of PD-related peritonitis. The incidence of peritonitis was higher than recommended range by ISPD in our population. Gram-positive organisms are the main causative agents of peritonitis and Gram-negative organisms are associated with a lower resolution rate and higher need for catheter removal. Determination of the etiology of each attack, and prevention of next episodes by directing intervention against any reversible risk factors are essential for preserving peritoneal membrane function and patient survival.

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ETHICS

Ethics Committee Approval: This study was approved by the University of Health Sciences Turkey, Hamidiye Clinical Research Ethics Committee (decision no: 5/53, date: 05.02.2021) and adhered to the principles of the Declaration of Helsinki.

Informed Consent: Informed consent was not obtained due to the retrospective design of the study.

Authorship Contributions

Concept: A.Ö., Design: S.Y.K., Data Collection or Processing: A.Ö., S.Y.K., Analysis or Interpretation: S.Y.K., Literature Search: A.Ö., Writing: A.Ö.

Conflict of Interest: The authors declare that they have no conflict of interest.

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