

Risk Factors for Continuous Ambulatory Peritoneal Dialysis Related Peritonitis

Sürekli Ayaktan Peritoneal Diyalizle İlişkili Peritonit İçin Risk Faktörleri

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ABSTRACT Objective: Peritonitis is a common clinical problem that occurs in patients with end stage renal disease and is treated by peritoneal dialysis. We evaluated the potential risk factors in continuous ambulatory peritoneal dialysis (CAPD) related peritonitis in our hospital. **Material and Methods:** The study was a case-control study. CAPD related peritonitis patients treated in Infectious Diseases and Clinical Microbiology Department between January 2005 and July 2006 formed the study group. The control group comprised CAPD patients without peritonitis. Demographic characteristics of the study and the control group were recorded. Potential risk factors for peritonitis were also recorded. Complete blood count and albumin levels were tested in both groups. Age, gender, hand washing habits, educational background, reason of renal disease, reason of CAPD who person performed CAPD, hemoglobin and albumin levels were investigated as potential risk factors by univariate and multivariate analyses. **Results:** There were 47 patients in the study group and 50 patients in the control group. The mean age of the patients was 49.6 ± 16.41 years and 44.82 ± 14.41 years in the study and control groups, respectively ($p > 0.05$). Anemia and low albumin level were found as risk factors in univariate analysis. Low albumin level ($p < 0.001$) was a statistically significant and independent risk factor for CAPD-related peritonitis in the multivariate analysis. It was found to increase the relative risk of peritonitis 11 fold. **Conclusion:** In several previous studies, low albumin level was reported as a risk factor in CAPD patients with peritonitis. Hipoalbuminemia can be considered an identifying parameter and the CAPD patients with hipoalbuminemia can be followed up closely for peritonitis.

Key Words: Peritoneal dialysis, continuous ambulatory; peritonitis; risk

ÖZET Amaç: Peritonit son dönem böbrek yetmezliği tanısı alan ve peritoneal diyaliz tedavisi uygulanan hastalarda sık görülen bir klinik problemdir. Biz bu çalışmada hastanemizde sürekli ayakta periton diyalizi (SAPD) ile ilişkili peritonit için risk faktörlerini araştırdık. **Gereç ve Yöntemler:** Çalışma vaka kontrol çalışması olarak gerçekleştirildi. Ocak 2005-Temmuz 2006 tarihleri arasında İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniğinde SAPD ile ilişkili peritonit tanısı ile izlenen hastalar çalışma grubu olarak alındı. Aynı dönemde SAPD uygulanan ancak peritoniti olmayan hastalar kontrol grubu olarak alındı. Çalışma ve kontrol grubunun demografik özellikleri kaydedildi ($p > 0.05$). Peritonit için potansiyel risk faktörleri kayıt altına alındı. Her iki grupta tam kan sayımı ve albumin düzeyi için tetkik yapıldı. Yaş, cinsiyet, el yıkama alışkanlığı, eğitim durumu, renal yetmezlik sebebi, SAPD yapılma sebebi, SAPD yapan kişi, hemoglobin ve albumin düzeyi tek değişkenli ve çok değişkenli analiz yöntemleri kullanılarak potansiyel risk faktörleri olarak incelendi. **Bulgular:** Çalışma grubuna 47, kontrol grubuna 50 hasta alındı. Çalışma ve kontrol grubundaki hastaların yaş ortalamaları sırası ile 49.6 ± 16.41 ve 44.82 ± 14.41 olarak bulundu ($p > 0.05$). Tek değişkenli analizde anemi ve albümin düzeyinin düşük olması peritonit riskini artıran faktörler olarak saptandı. Albümin düzeyinin düşük olması çok değişkenli analizde de anlamlı bulundu ($p < 0.001$) ve albümin düzeyi düşük olan hastalarda SAPD ilişkili peritonit riskinin 11 kat daha fazla olduğu belirlendi. **Sonuç:** Daha önce yapılmış birkaç çalışmada düşük albümin düzeyi SAPD hastalarında peritonit için risk faktörü olarak bildirilmiştir. SAPD hastalarında hipoalbüminemi peritonit oluşması açısından belirleyici bir parametre olarak değerlendirilebilir ve albümin düzeyi düşük olan SAPD hastaları peritonit yönünden yakından izlenebilir.

Anahtar Kelimeler: Periton diyalizi, sürekli ayakta periton diyalizi; peritonit; risk

Peritoneal dialysis has been increasingly used in end-stage renal disease for the last 60 years.¹ The high incidence rate of peritonitis in the earlier years has gradually decreased owing to the innovation of Tenckhoff catheter and improved techniques.¹⁻³ However, peritonitis is still a common clinical problem that occurs in patients treated by peritoneal dialysis.⁴⁻⁷ Multiple peritonitis episodes may result in ending the continuous ambulatory peritoneal dialysis (CAPD) program and necessitate use of treatment modalities such as hemodialysis, which would render the patient more dependent.^{4,5} In previous studies, black race, diabetes mellitus (DM), and low albumin levels were determined as the risk factors for peritonitis in CAPD patients.^{8,9} In these patients, the knowledge of risk factors for peritonitis will be beneficial for prevention of peritonitis and determination of appropriate early treatment. This study aimed to determine risk factors for CAPD-related peritonitis.

MATERIAL AND METHODS

SETTING AND STUDY PERIOD

A case-control study was conducted in the peritoneal dialysis unit of nephrology department and infectious diseases and clinical microbiology department of Ankara Training and Research Hospital, Turkey. The study period was from January 2005 to July 2006.

PATIENTS

The study involved 47 patients with CAPD-related peritonitis who applied to Ankara Training and Research Hospital between January 2005 and July 2006. Only the patients who have first peritonitis episode were included. In the same period, 50 patients who were also enrolled in CAPD program without any previous episodes were selected as the control group. In all the patients, standard Tenckhoff catheter was used, and in most, "double bag connecting system" was used. Peritoneal dialysis fluid was lactate-based dialysate with glucose concentrations ranging from 1.5 to 4.25 g/L. Patients performed four exchanges per day with 2 L.

The patients and/or their relatives were trained by dialysis nurses for peritoneal dialysis application.

For the patients with peritonitis the complaints, physical examination and laboratory findings, peritoneal fluid cell count, the results of direct microscopy and culture of peritoneal fluid as well as the antibiotic sensitivity of the isolated agent were recorded. After the samples were obtained for microbiological evaluation, in all the patients, empirical cefazoline and gentamicin were started. The treatment was modified depending on the culture results. The patients were followed-up until the end of their treatment, or until they expired.

DIAGNOSIS OF PERITONITIS

The diagnosis of peritonitis was based on at least two of the following criteria: abdominal pain or cloudy peritoneal dialysate effluent, leukocytosis in peritoneal fluid effluent (white cell count: at least 100/mm³), or positive Gram stain or culture of effluent.¹⁰ Bacterial culture was performed using BactAlert bottle and direct inoculation.

RISK FACTORS

The potential risk factors for peritonitis were recorded in both groups. The age, gender, hand washing habits, educational background, primary renal diseases, the reason of CAPD and the person who performed CAPD (CAPD was performed by patient or by relatives) were recorded and investigated as potential risk factors for CAPD-related peritonitis. The patients or their relatives who performed CAPD were asked for whether they washed their hands before CAPD. Hemoglobin and albumin levels were also recorded and investigated as potential risk factors.

STATISTICAL ANALYSIS

All the statistical analyses were performed through SPSS 13.0 software. All the data were expressed as mean \pm SD for normally distributed data, and median or range for skewed data. The Chi-square or Fisher's exact test was used in univariate analysis. Student's t test was used for continuous variables. Stepwise logistic regression analysis was undertaken to control the effects of confounding variables. All the variables found to be significantly ($p < 0.05$) associated with peritonitis in the univariate analysis were entered into the multiple regression model.

RESULTS

Twenty-nine microorganisms were isolated in 47 peritonitis episodes. In the evaluation of peritoneal fluid cultures (Table 1), *Staphylococcus* species (48.3%) were the most common, followed by gram-negative microorganisms (24.1%), among those isolated.

The variables recorded as potential risk factors were studied with univariate analysis; The person performed CAPD, anemia and low albumin levels were factors of statistical significance (Table 2). All of the patients or relatives who are performed CAPD told that they washed their hands before each CAPD, in the study and control group.

The variables that were determined as statistically significant risk factors for CAPD-related peri-

Microorganism	Number	%
Coagulase-negative <i>Staphylococci</i>	9	31.3
<i>Staphylococcus aureus</i>	5	17.2
<i>Klebsiella</i> spp.	2	6.9
<i>Pseudomonas</i> spp.	2	6.9
<i>Enterococcus</i> spp.	2	6.9
<i>Streptococcus</i> spp.	3	10.3
Other*	6	20.7
Total	29	100.0

*One *Acinetobacter* spp., one *Candida albicans*, one *Cellulomonas* spp., one *Difteroid* spp., one *Enterobacter* spp., one *Micrococcus* spp.

tonitis in univariate analysis were also studied through stepwise logistic regression analysis. The person performed CAPD and anemia were not

TABLE 2: Risk factors for peritonitis (Univariate Analysis).

Risk factors (n)	Patient group (n= 47) n (%)	Control group (n= 50) n (%)	p	OR	95% CI
Age	49.06 ± 16.41	44.82 ± 14.41	>0.05		
Gender					
Female	16 (34)	25 (50)	>0.05	1.9	0.85-4.39
Male	31 (66)	25 (50)			
Education					
Primary school	38 (80.9)	38 (76)	>0.05	1.33	0.50-3.53
High school	9 (19.1)	12 (24)			
Reason of CAPD					
Patient preference	43 (91.5)	45 (90)	>0.05	1.2	0.30-4.74
Failure of vascular access	4 (8.5)	5 (10)			
Hand washing ^{a,b}	50 (100)	50 (100)			
Person performed CAPD					
Patient	31 (66)	42 (84)	<0.05	2.7	1.03-7.13
Relative of the patient	16 (34)	8 (16)			
Reason of renal disease					
Hypertension	9 (19.1)	9 (18)	>0.05	1.38	0.93-2.04
Diabetes mellitus	7 (14.9)	4 (8)			
Hypertension+diabetes mellitus	9 (19.1)	6 (12)			
Other	1 (2.1)	10 (20)			
Unknown	21 (44.7)	21 (42)			
Laboratory parameters					
Anemia ^c	41 (87.2)	33 (66)	<0.01	1.7	1.2-2.3
Low albumin level (<3.4 g/dl)	35 (74.5)	10 (20)	<0.001	3.46	1.96-6.1

CAPD: Continuous ambulatory peritoneal dialysis

^a Because the parameters studied were found 100% in both groups, no statistical evaluation could be performed.

^b The patients or relatives who are performed CAPD were asked for if they wash their hands before CAPD

^c Hb level <13 g/dL for male, <12 g/dL for female.

statistically significant in this analysis. These parameters were not found as risk factors. The analysis revealed that low albumin level was a statistically significant and independent risk factor for CAPD-related peritonitis (p= 0.000, RR: 11.01, 95% CI: 4.17-29.14) (Table 3).

DISCUSSION

CAPD is one of the dialysis methods that renders the patients less dependent and thus increases the life quality of end-stage renal patients. More than 110.000 chronic renal failure patients in the world received CAPD by 2000.¹¹

Peritonitis has been one of the most important complications arising from CAPD application.^{4,5} In this patient group, peritonitis leads to complications such as extended hospitalization, technical failure, peritoneal membrane damage, need for hemodialysis and death.¹² The incidence rate for peritonitis varies among the centers with 0.2-0.7 episodes reported per year.¹³⁻¹⁶

In two major studies on peritonitis, Farias et al determined the race, and McDonald et al determined “body-mass index” as independent risk factors for peritonitis.^{17,18} In addition to these two factors, high levels of humidity and heat, black race, low educational level, the system type used for peritoneal dialysis, young age (< 20), nasal carriage of *S. aureus*, Ultra set Exchange system, intermittent rifampicin treatment, DM, anemia and hypoalbuminemia have been reported to increase the risk for peritonitis.^{9,19-23}

Hand washing is a key to prevent contamination. Patients should be instructed to never begin PD connection before appropriate hand washing and until hands are thoroughly dry.²⁴ In our study, hand washing habits was not investigated as a risk

factor because all of the patients or relatives told that they washed their hands before each CAPD.

In our study, the educational level of the patient group was lower than that of the control group. However, the differences between the groups were not statistically significant.

Chow et al conducted a study on 246 CAPD patients and reported higher risk of peritonitis in CAPD patients with DM.⁹ In addition, peritonitis incidence caused by gram negative microorganisms was significantly higher in this patient group.⁹ In other two studies investigating risk factors for peritonitis, DM was not found as a risk factor.^{17,21} In our study, the incidence rate of DM among peritonitis patients (34%) was higher than in the control group (20%); however, the difference was not statistically significant.

The relationship between hypoalbuminemia and peritonitis is not clearly shown. In some studies, severe peritonitis has been reported to lead to hypoalbuminemia.²⁵ In others, however, hypoalbuminemia has been reported as a risk factor for peritonitis.^{9,23,26} Nevertheless, there are some studies reporting the contrary.¹⁷

Hypoalbuminemia was reported as a risk factor for peritonitis in the study of Chow et al.⁹ In the study of Wang et al on 393 patients who were treated by peritoneal dialysis, low serum albumin level was reported to be a risk factor for peritonitis, but no explanation was provided for the relationship between the low albumin levels and peritonitis.²⁶ The same result was obtained in the study of Sirvongs et al, and each 1 g/dL decrease in the albumin level was found to cause 27% increase in the risk for peritonitis.²³ The authors attributed hypoalbuminemia to malnutrition and claimed that interventions for malnutrition might decrease the risk for infection. Hypoalbuminemia has been associated with inflammatory response, and inflammation due to metabolites resulting from uremia and increased oxidative stress in patients with chronic renal failure have been reported to reduce albumin levels.²³ In our study, upon logistic regression analysis, hypoalbuminemia has been detected as a

TABLE 3: Risk factors for peritonitis (Multivariate Analysis).

Risk factor	p	OR	95% CI
Person performed CAPD	>0.05	2.13	0.68-6.69
Anemia	>0.05	2.98	0.89-9.94
Low albumin level (<3.4 g/dl)	<0.001	11.01	4.17-29.14

CAPD: Continuous ambulatory peritoneal dialysis.

risk factor for peritonitis in the patients undergoing CAPD treatment ($p < 0.05$).

Hipoalbuminemia has also been investigated in children enrolled in CAPD program. In a Canadian study involving 180 children, the comparison of the children with hypoalbuminemia and those without revealed lower albumin levels in the first month of peritoneal dialysis and two or more episodes of peritonitis. The authors have concluded that peritonitis could be a predictor for low serum albumin.²⁵

Heaf et al conducted a study on 155 peritoneal dialysis patients in Denmark, the results of which seem to contribute to the understanding of mechanism underlying the peritonitis and hypoalbuminemia association.²⁷ They reported that in a group of patients, hypoalbuminemia was due to peritoneal albumin loss resulting from peritoneal dialysis. The loss of albumin was accounted for by “bathing” effect, and since it was associated with peritoneal dialysis, it has been claimed to be iatrogenic. In the patient group with high peritoneal “large por fluid flux” values, significant levels of hypoalbuminemia were shown soon after peritoneal dialysis application was started. In the two ye-

ar follow-up, however, no relationship was detected between the high “large por fluid flux” values and peritonitis. On the other hand, in the same patient group, a significantly higher mortality rate was noted, and increased risk of death for this group was attributed to increased risk for infection. The authors have also asserted a possibility of peritoneal immunoglobulin loss. Peritonitis was detected in eight of 16 patients who died from infections. Hypoalbuminemia was held responsible for inducing hypercoagulation and endothelial dysfunction, and contributing malnutrition-inflammation-atherosclerosis syndrome.²⁷

In conclusion, low albumin levels in three earlier studies were reported to increase the risk for peritonitis.^{9,23,26} In one study, on the other hand, hypoalbuminemia was not found to be a risk factor.¹⁷ In our study, lower albumin levels of the patients could be predictive for peritonitis risk, supporting the hypothesis that interventions for low albumin level might decrease the risk for peritonitis. To explain the relationship between hypoalbuminemia and peritonitis, further studies are including immunological markers with more patients must be performed.

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