Evaluation of Peritonitis Incidence, Etiology, Associated Factors and Prognosis of Continuous Ambulatory Peritoneal Dialysis Patients

Sürekli Ambulatuar Periton Diyalizi Hastalarında Peritonit Sıklığı, Etiyolojisi, İlişkili Faktörler ve Prognozun Değerlendirilmesi

ABSTRACT

OBJECTIVE: Peritonitis is the most important complication of peritoneal dialysis (PD). We evaluated the incidence of peritonitis, active microorganisms and their susceptibility profile and determine prognosis.

MATERIAL and METHODS: One hundred fifty three PD patients were evaluated for aetiology, drug usage, accompanying disease, type, duration and personal preference for PD, care-giver, protein catabolic rate (PCR), residual urine volume, ultrafiltration volume, type of peritoneal membrane transport and baseline laboratory values.

RESULTS: The incidence of peritonitis was 0,284 attack/patient/year. The most common organisms were coagulase negative staphylococci (18.3%) followed by S. aureus (14.8%) and gram-negative bacillus (13.1%).

Peritonitis was more common in elderly, those with longer PD duration, low residual urine volume, patients with low PCR and hepatitis C. However, patients using erythropoietin and automated PD had low incidence of peritonitis compared to others.

Mortality rate was higher in gram-negative and fungal peritonitis and prognosis was worse in gram-negative peritonitis

CONCLUSION: Peritonitis incidence and aetiology were compatible with literature. One must be careful to protect residual renal function (RRF) as peritonitis incidence was significantly reduced in patients with RRF. PCR values were significantly lower in peritonitis. Adequate protein intake and nutritional support may be important in this respect.

KEY WORDS: Hepatitis C, Peritoneal dialysis, Peritonitis, PCR, Residual renal function

ÖZ

AMAÇ: Peritonitler, periton diyalizinin (PD) en önemli komplikasyonudur. Merkezimizde izlenen peritonit ataklarının incelenmesi, peritonit sıklığı, etken mikroorganizma dağılımı, duyarlılık profili ve prognozun değerlendirilmesi amaçlanmıştır.

GEREÇ ve YÖNTEMLER: Yüzelliüç PD hastası, son dönem böbrek yetmezliği etiyolojisi, kullandığı ilaçlar, eşlik eden hastalıklar, PD dozu, tipi, tercih nedeni ve süresi, değişimi yapan kişi, protein katabolik hız (PCR), rezidüel idrar miktarı, ultrafiltrasyon miktarı, periton membranının transport tipi, bazal laboratuvar değerleri açısından değerlendirilmiştir.

BULGULAR: Son 11 yıllık peritonit sıklığımız; 0,284 atak/yıl/hasta olarak hesaplanmıştır. En sık peritonit etkeninin koagülaz negatif stafilokoklar (% 18,3) olduğu, bunu sırasıyla S. aureus (%14,8) ve gram negatif basillerin (%13,1) izlediği görülmüştür.

Peritonit; yaşlılarda, PD uygulama süresi uzun olanlarda, Hepatit C infeksiyonu olanlarda, rezidüel idrar miktarı ve PCR değeri düşük olanlarda daha sık saptanmıştır. Eritropoetin kullananlarda ve aletli PD uygulayanlarda peritonit sıklığı diğerlerine göre daha düşük bulunmuştur.

Gram negatif bakteri ve mantarların etken olduğu peritonitlerde mortalite (%17,4) daha yüksek bulunmuş; prognozun gram negatif peritonitlerde daha kötü olduğu görülmüştür.

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SONUÇ: PD hastalarımızda peritonit sıklığı ve etiyolojisi uluslararası literatürle benzer bulunmuştur. Rezidüel renal fonksiyon (RRF) korunan hastalarda peritonit sıklığının anlamlı düşük bulunması nedeniyle RRF'nin korunmasına daha fazla özen gösterilmesi gerekmektedir. PCR değeri peritonitlilerde anlamlı düşük bulunmuştur. Yeterli protein alımı ve beslenme desteği bu açıdan önemli olabilir.

ANAHTAR SÖZCÜKLER: Hepatit C, Periton Diyalizi, Peritonit, PCR, Rezidüel renal fonksiyon

INTRODUCTION

Peritoneal dialysis (PD) is an alternative therapy to haemodialysis (1). Despite recent advances, peritonitis continues to be the most important complication of PD. Catheter exit site infection, tunnel infection and peritonitis are important reasons of morbidity and mortality in CAPD patients (2). Peritonitis associated with PD is most often due to contamination with pathogenic skin bacteria, with Staphylococcus epidermidis and S. aureus accounting for the majority of cases (3).

Empiric antibiotic therapy should cover both gram-positive and gram-negative bacteria. The guideline of International Society of Peritoneal Dialysis (ISPD) recommends that the microorganisms and their susceptibility profile in each centre should be kept in mind when to institute empirical therapy (4). For this reason, all centres must collect data from their patients.

We evaluated the incidence of peritonitis, active microorganisms and their susceptibility profile and tried to determine the factors influencing prognosis.

MATERIAL and METHOD

One hundred fifty three patients who have been followed from 1998 to 2009 in Suleyman Demirel University Department of Nephrology have been chosen and patients who have received less than 6 months of PD therapy were excluded from the study. We evaluate the aetiology of end-stage renal disease, accompanying disease, drug usage, the exact reason of preference of peritoneal dialysis, duration of dialysis, care-giver, the type of PD, protein catabolic rate (PCR), dose of dialysis (Kt/V), residual urine volume, ultrafiltration volume, type of peritoneal membrane transport, baseline laboratory values and the risk factors for the development of peritonitis.

Diagnosis of peritonitis depended on at least two of the following statements:

1. Signs and symptoms of peritoneal inflammation

2. Elevated leukocyte (>100/mm^3) or neutrophil (>50%) count associated with blurry peritoneal fluid

3. Demonstrating the presence of microorganism with either Gram stain or culture.

Empirical therapy was begun initially and subsequent changes were made depending on culture results. Symptoms on the beginning of infection, site of infection, time from initiation of PD to peritonitis development, laboratory values, cell count in peritoneal fluid, culture results, antibiotic susceptibility, therapy, its results and outcome were evaluated in this study.

STATISTICAL ANALYSIS

Student's t-test was used for comparison of the means of two groups and chi square test was performed to detect the difference between two groups. Logistic regression analysis was used to evaluate the significant risk factors for peritonitis. SPSS version 15.0 was used in all statistical analysis. For all comparisons, P<0.05 was considered significant.

RESULTS

In the last 11 years, 175 attack of peritonitis were detected and the incidence of peritonitis was 0.284 attack/year/patient. The most prominent organism was coagulase negative Staphylococci (18.3%) followed by S. auerus (14.8%) and gram-negative bacilli (13.1%). 35.4% of attacks were culture negative (Table I).

Eighty-six patients were found to have peritonitis (45 women and 41 men) and the median age of the patients was 54.2±13.22 years. 67 patients (34 men and 33 women) suffered no attack and median age of the group was 47.47±16.86 years. Median age in peritonitis group was found to be significantly older compared to other group (p=0.008).

The distribution of the patients for education level is shown in Figure 1. Education level and peritonitis incidence were inversely correlated and found to be statistically significant (p=0.046, Table II).

Hypertension was the most common reason of chronic renal failure (34%), it was followed by diabetes (32%), glomerulonephritis (16%) and pyelonephritis (6%) and none of them is associated with peritonitis (p=0.327).

Residual urine volumes were 544,93±651,20 ml with peritonitis and 830,08±722,24 ml without peritonitis. Peritonitis were more common with low PCR, low residual urine volume and long PD duration (p=0.038, 0.018 and 0.001 respectively).

CAPD was performed for 134 patients (87.6%) and the rest of them (19 patients 12.4%) performed automated peritoneal dialysis (APD). Peritonitis incidence was significantly low with APD (p=0.026, Table III).

Peritonitis incidence was found to be significant in hepatitis C but not in patients with hepatitis B (p=0.047 and 0.407 respectively).

Table I: The distribution of microorganisms associated with peritonitis.

Pathogen	n	%
CNS	32	18.3
MSCNS	20	11.4
MRCNS	12	6.9
S. aureus	26	14.8
MSSA	20	11.4
MRSA	6	3.4
Gram-negative	23	13.1
Streptococcus	12	6.9
Yeast	9	5.1
Enterococcus	4	2.3
Group D streptococcus	3	1.7
Tbc	2	1.1
Gram-positive rod	2	1.1
Non-cultured	62	35.4
Total	**175**	**100**

Table II: Association between peritonitis and educational level of patients.

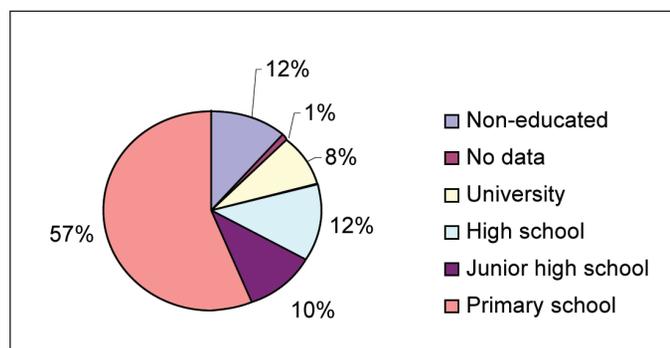| Educational level		Peritonitis		Total
		Yes	No	
Non-educated	n	15	3	18
	%	83.3	16.7	100
Primary School	n	48	38	86
	%	55.8	44.2	100
Junior high school	n	10	6	16
	%	62.5	37.5	100
High school	n	9	10	19
	%	47.4	52.6	100
University	n	4	9	13
	%	30.8	69.2	100
Total	**n**	**86**	**66**	**152**
	%	**56.6**	**43.4**	**100**

Chi-square test. p=0,046

EPO usage was 29.4% and 45.6% in peritonitis and non-peritonitis group consequently. EPO usage was found to decrease the incidence of peritonitis (p=0.044) but the significance was lost with logistic regression analysis (p=0.061).

Table III: Type of change of peritoneal dialysis fluid and its impact on incidence of peritonitis.

Type of change		Peritonitis		Total
		Yes	No	
CAPD	n	80	54	134
	%	59.7	40.3	100
APD	n	6	13	19
	%	31.6	68.4	100
Total	**n**	**86**	**67**	**153**
	%	**56.2**	**43.8**	**100**

Chi-square test. p=0,026

Figure 1: Distribution of patients by educational level.

The most common symptoms of peritonitis were abdominal pain (89%), nausea (43.4%), blurry dialysate (40.6), vomiting (25.7%) and fever (22.3%) in our study. Median leukocyte and neutrophil count were $2928.81 \pm 3435.13/mm^3$ and $2218.44 \pm 3013.16/mm^3$ in dialysate.

Of 175 attack of peritonitis, 146 (83.4%) recovered whereas in 17 patients (9.7%) peritoneal dialysis was terminated and switched to haemodialysis and 12 (6.9%) died. The mortality rate was higher in patients with gram-negative bacteria or fungal peritonitis compared to others; we observed that prognosis was worse in gram-negative peritonitis than in gram-positives (p=0.0001, Table IV).

DISCUSSION

Peritonitis is the most important complication of CAPD and its treatment requires knowing the microorganism and the susceptibility profiles (5). The peritonitis incidence was found to be 0.327 attack/year/patient in 3111 CAPD patients and 0.434/attack/year/patient in 6544 CAPD patients in separate studies (6). In this study, it was 0.284/attack/year/patient. Bulut et al found that microorganisms associated with peritonitis were coagulase negative staphylococci, S. aureus and E. coli in 56 CAPD patients (5). Kaya et al showed that the rate of gram-positive

Table IV: Association with active microorganisms and results of treatment.

Culture		Result of treatment			Total
		Cure	Pd end	Ex	
Gram-positive	n	72.0	2.0	5.0	79.0
	%	91.1	2.5	6.3	100.0
Gram-negative	n	16.0	3.0	4.0	23.0
	%	69.6	13.0	17.4	100.0
Yeast	n	0.0	8.0	1.0	9.0
	%	0.0	88.9	11.1	100.0
Tbc	n	1.0	1.0	0.0	2.0
	%	50.0	50.0	0.0	100.0
Total	**n**	**89.0**	**14.0**	**10.0**	**113.0**
	%	**78.8**	**12.4**	**8.8**	**100.0**

Chi-square test. p= 0,0001

bacteria was 68.2% and gram-negative bacteria 24.8% with coagulase-negative staphylococci the most common observed microorganism in 115 patients (7). Incidence and aetiology of peritonitis were in correlation with the literature in our study. 35.4% of attacks were culture negative. ISPD recommends that 50 ml of fluid be centrifuged and sediment cultured. Also, according to ISPD, culture negativity should be less than 20% (4). We speculated that application of ISPD recommendations might affect culture results and lower culture negativity.

In an international cooperative study (Canada-China), peritonitis incidence was lower in Chinese patients than in Canadians. It was interpreted that lower age and lack of coexisting diseases were the factors that protect Chinese from peritonitis; older age and hypoalbuminemia were correlated with peritonitis (8). We found a significant relationship between older age and peritonitis (p=0.008).

Huang et al, compared complications associated with the PD method in 247 patients. Peritonitis incidence was significantly lower in APD compared to CAPD patients (p<0.001) and diabetes had no impact on peritonitis (9). Newly developed Y systems and new communications systems that operate with "washing before filling" lowered the peritonitis incidence in CAPD patients (10). We, too, found that peritonitis incidence was significantly lower in APD compared to CAPD patients (p=0.026) and diabetes had no impact on peritonitis.

In a study of 79 patients, malnutrition was observed in 34% and peritonitis was more common in malnourished patients (p<0.05) (11). Sarıkaya et al showed a significant correlation between low peritonitis index (patients who had less than two peritonitis attacks in a year) and high serum albumin levels

(p=0.04). PCR and Kt/V were higher in patients with low peritonitis index but this was not statistically significant (12). We found that the basal PCR rate, which was associated with dietary protein amount and nutritional status, was lower in peritonitis and this was consistent in the literature (p=0.038).

The reduction in residual renal function (RRF) was correlated with hypervolemia, anaemia, inflammation, malnutrition and mortality. Han et al found that, RRF was lower in peritonitis (p<0.01) and time to first peritonitis attack was significantly longer in high RRF patients (p<0.001). RRF lost and diabetes were associated with peritonitis development (13). In our study, low residual urine was associated with more common attacks and RRF lost was a risk factor for development of peritonitis (p=0.018). The exact protective mechanism in preservation of RRF is not clear; clearance of immunosuppressive uremic toxins with naive kidneys may have a role.

Incidence of peritonitis was higher with HCV infection. Defects in cellular immune response, delay in T cell CD4 and CD8 responses, ineffectiveness in effector T cells and failure in antigen presentation were the factors thought to be responsible for this situation (14). Similar mechanisms also played role in hepatitis B infection; we speculated that due to low number of patients, we didn't find significant increase in Hepatitis B.

Gram-negative organisms, mycobacterium species, fungal peritonitis, polymicrobial peritonitis and low residual filtration rate were associated with poor prognosis (15). We also showed that, low residual filtration rate, gram-negative bacteria and fungal peritonitis were significant factors affecting prognosis and mortality.

CONCLUSION

In this study, peritonitis incidence and aetiology were found to be similar to the international literature. Our empirical treatment of choice was found to be suitable when pathogen variation and their susceptibility profile were evaluated at our centre. Peritonitis was more common in the elderly, those with low PCR and hepatitis C. However, patients using erythropoietin and automated PD had a low incidence of peritonitis compared to CAPD. The mortality rate was higher in gram-negative and fungal peritonitis and prognosis was worse in gram-negative than gram-positive peritonitis. One must take care to protect residual renal function (RRF) as peritonitis incidence was significantly reduced in patients with "protected" RRF. PCR values, which reflected the nutritional status of patients, were significantly lower in patients with peritonitis. Adequate protein intake and nutritional support may be important in this respect. Prospective studies are needed to better identify the risk factors for peritonitis.

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