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Vancomycin Therapy for Treatment of Peritonitis in Outpatients on Peritoneal Dialysis

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ABSTRACT

Vancomycin therapy is frequently used for peritonitis in patients on peritoneal dialysis, but the emergence of resistance has been reported. We evaluated the efficacy of a single intraperitoneal dose of vancomycin for peritonitis in peritoneal dialysis patients. We assessed 24 episodes of peritonitis in 16 patients, and compared clinical parameters between responders and nonresponders. Vancomycin was effective for 12 patients (18 out of 24 episodes, 75.0%). Nonresponders had a significantly higher initial C-reactive protein level and dialysis fluid leukocyte count, and the mean serum albumin over three months before onset was significantly lower than in responders. Patients with a serum albumin level 3.0 g/dl or more were significantly more likely to respond than those with a level less than 3.0 g/dl. In conclusion, it seems reasonable for peritonitis patients with a mild inflammatory response and a serum albumin 3.0 g/dl or more to receive intraperitoneal vancomycin on an outpatient basis.

Key words: *Continuous ambulatory peritoneal dialysis, Dialysis-related peritonitis, Vancomycin*

Peritonitis is an important complication that may cause withdrawal from continuous ambulatory peritoneal dialysis (CAPD), since it can induce sclerosing encapsulating peritonitis and peritoneal hypofunction[3]. We performed treatment for CAPD peritonitis with a single intraperitoneal dose of vancomycin in order to achieve an early cure on an outpatient basis. The present study retrospectively evaluated the therapeutic results, side effects, and influence on ultrafiltration of this therapy. A comparison was also made between patients who were responsive and unresponsive to treatment.

MATERIALS AND METHODS

Subjects: The subjects were 16 patients on CAPD attending the Second Department of Internal Medicine at Hiroshima University School of Medicine who developed peritonitis between July 1991 and October 1996 (24 episodes in all). The diagnosis of peritonitis was made on the basis of a cloudy dialysate associated with a dailysis fluid leukocyte count of 100/mm^3 or more. The patients comprised ten men (18 episodes) and six women (six episodes) aged from 35 to 66 years (mean: 54.1±8.1 years). The underlying cause of chronic renal failure was chronic glomerulonephritis in 14 patients, nephrosclerosis in one, and diabetic nephropathy in one. The duration of CAPD at the onset of peritonitis was 3 to 113 months (mean: 39.2±27.8 months).

Management of peritonitis: When peritonitis developed, the dialysis fluid was cultured for bacteria, and the abdominal cavity was washed two to three times with fresh dialysis fluid. Then vancomycin (30 mg/kg) was given intraperitoneally once via a dialysis bag. After 6 hours, the dialysis fluid was changed and patients were returned to routine CAPD. If they had only mild abdominal pain (a symptom of peritonitis), they were not admitted to hospital. The response to therapy was assessed from the turbidity of the dialysis fluid, the dialysis fluid leukocyte count of less than 100/mm^3, and the presence or absence of an improvement in symptoms. If vancomycin failed to reduce the cloudiness of the dialysis fluid and the cell count within three days after treatment, it was judged ineffective and other antibiotics were added.

The patients were classified as responders or nonresponders. These two groups were compared with respect to the peripheral blood leukocyte count, C-reactive protein (CRP) value at the onset of peritonitis, the dialysis fluid leukocyte count, and the mean serum creatinine and albumin levels over three months before the onset. Comparisons were done using the unpaired t-test

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Table 1. Relationship between clinical parameters and VCM therapy

Clinical parameter	Response to VCM	mean±SD	p value
Peripheral blood white cell count, /mm³	Yes	9938.9±786.3	NS
	No	11160.0±1561.3	
CRP, mg/dl	Yes	5.5±1.3	p<0.01
	No	12.7±4.8	
Dialysis fluid leukocyte count, /mm³	Yes	707.2±180.5	p<0.05
	No	6438.8±490.5	
Serum creatinine, mg/dl	Yes	10.6±2.1	NS
	No	13.1±4.2	
Serum albumin, g/dl	Yes	3.4±0.3	p<0.01
	No	2.6±0.4	

Table 2. Relationship between serum albumin level and VCM therapy

Albumin	Response to VCM	
	Yes	No
3.0 g/dl or more	17	1
less than 3.0 g/dl	1	4

χ^2=12.75, p<0.001

or χ^2-test, and p<0.05 was taken to indicate significance.

RESULTS

The symptoms of peritonitis were fever in 11 patients (14 episodes), abdominal pain in 14 patients (19 episodes), and cloudy dialysis fluid in 16 patients (24 eipsodes). Laboratory studies showed a peripheral blood leukocyte count of 5800–17900/mm³ (mean: 10400.2±693.9/mm³), a CRP of 0.3–44.3 mg/dl (mean: 8.6±1.9 mg/dl), and a dialysis fluid leukocyte count of 108–26000/mm³ (mean: 1937.7±1067.3/mm³). Dialysis fluid cultures were positive for bacteria in seven patients (eight out of 24 episodes, 33.3%). Causative organisms included *Staphylococcus aureus* in two episodes, *α-streptococcus* in two, *Enterococcus faecalis* in one, *Staphylococcus epidermidis* in one, *Staphylococcus simulans* in one, and *Citrobacter freundii* in one episode.

Of the 16 patients with CAPD-associated peritonitis, 12 patients (18 out of 24 episodes, 75.0%) showed improvement after vancomycin therapy. Among eight episodes of culture-positive peritonitis, seven showed improvement after vancomycin therapy. Among the 16 episodes of culture-negative peritonitis, 11 showed improvement, so there was no difference in effectiveness between the two groups. Among these 12 patients, two were hospitalized to monitor vancomycin levels at the start of this regimen and one was admitted because of complicating aplastic anemia, while the others remained as outpatients. There were no side effects from the vancomycin therapy. On the other hand, all patients unresponsive to vancomycin required hospitalization. Of the six nonresponders, four patients (4 out of 6 episodes) showed improvement after treatment with other antibiotics. In addition, one patient was changed to hemodialysis and one died of sclerosing encapsulating peritonitis. Ultrafiltration was preserved after three months in all vancomycin responders, but temporary depression of ultrafiltration was observed in 4 of the 6 nonresponders.

In the nonresponders, excluding a patient positive on culture for *Citrobacter freudii* as a gram-negative bacterium, the CRP and the dialysis fluid leukocyte count were significantly higher than those in the responders, and the serum albumin of the nonresponders was significantly lower than that of the responders (Table 1). Patients with a serum albumin level of 3.0 g/dl or more showed a significantly better response to vancomycin than those with a serum albumin level of less than 3.0 g/dl (Table 2).

DISCUSSION

CAPD has a number of merits over hemodialysis, including less impact on daily life, but the risk of peritonitis cannot be overlooked. The major problem associated with peritonitis is transient depression of ultrafiltration, which necessitates frequent use of dialysis fluid with a high concentration. This induces peritoneal hypofunction, occasionally leading to fatal complications such as sclerosing peritonitis and sclerosing encapsulating peritonitis[4]. Hence, treatment of peritonitis in CAPD patients often requires hospitalization, which interferes with daily life and places a financial burden on the patient. Vancomycin is bactericidal for gram-positive organisms, and is effective against methicillin-resistant *Staphylococci*. Because most organisms causing CAPD peritonitis are gram-positive bacteria, vancomycin has been frequently used to treat it[1,5,8,10]. It is known that a single intraperitoneal dose of vancomycin results in effective blood levels against gram-positive organ-

isms that are maintained for at least one week[9,10], and this was also confirmed at our department (data not shown). Of the 24 episodes with peritonitis, 18 showed a response to therapy and most of them did not require hospitalization. Causative organisms were only identified in 8/24 episodes of peritonitis (33.3%), but 11 out of 16 episodes of culture-negative peritonitis (68.8%) showed improvement after vancomycin therapy. Thus, vancomycin had an excellent therapeutic effect on culture negative patients, too. After intraperitoneal administration of vancomycin, the development of chemical peritonitis and auditory disturbance have been reported[14,15], and the induction of peritoneal dysfunction has been suspected. However, intraperitoneal administration of vancomycin has also been reported to be safe and to have no effect on peritoneal function[2]. In the present study, no side effects were caused by a single peritoneal dose of vancomycin, and there was no depression of ultrafiltration after either 3 or 6 months. Vancomycin resistance has increased recently, and this has led to abandoment of its routine or empirical use for CAPD peritonitis by an increasing number of institutions[6,7,11–13].

Our retrospective study also showed that the CRP at the onset of peritonitis and the dialysis fluid leukocyte count were significantly greater in the patients who were unresponsive to therapy than in the responders. The mean serum albumin level over three months before the onset of peritonitis was significantly lower in the nonresponders. Accordingly, for patients with an increase of CRP and dialysis fluid leukocytes, indicating marked inflammation, as well as patients with a serum albumin level of less than 3.0 g/dl, suggesting undernutrition, our outpatient treatment protocol should be abandoned and be replaced by inpatient treatment. In the present study, although we administered vancomycin before identification of the causative organisms, vancomycin therapy appeared to achieve satisfactory results. In conclusion, in the presence of a mild inflammatory reaction and a serum albumin level of 3.0 g/dl or more, it may still be reasonable to treat patients with a single intraperitoneal dose of vancomycin on an ambulatory basis.

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