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Cefazolin plus netilmicin versus cefazolin plus ceftazidime for treating CAPD peritonitis: Effect on residual renal function

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Cefazolin plus netilmicin versus cefazolin plus ceftazidime for treating CAPD peritonitis: Effect on residual renal function.

Background. The International Society for Peritoneal Dialysis (ISPD) treatment guidelines for continuous ambulatory peritoneal dialysis (CAPD) peritonitis 2000 recommended the use of cefazolin plus ceftazidime as the initial empirical therapy in patients with residual renal function (RRF). However, this treatment regimen has not been compared with the conventional regimen of cefazolin plus netilmicin in prospective, randomized controlled trials.

Methods. Stable CAPD patients who developed clinical evidence of peritonitis were randomized to receive intraperitoneal (i.p.) cefazolin plus netilmicin or cefazolin plus ceftazidime once daily in the long dwell for 14 days. For patients with RRF (>1 mL/minute) before entry into the study ($N = 50$), RRF and 24-hour urine volume were measured at days 1, 14, and 42 after commencement of i.p. antibiotic treatment.

Results. One hundred and two patients were recruited into the study. The primary cure rates of i.p. cefazolin plus netilmicin and cefazolin plus ceftazidime were 66.7% and 64.7%, respectively. The overall cure rate for the 2 treatment regimens was 82.3% for both. Seven patients (14%) from each treatment group required removal of the dialysis catheters due to treatment failure. Relapse of peritonitis occurred in 2 patients (4%) in both treatment groups. Thirty-six patients with RRF at baseline achieved primary cure of their peritonitis by the assigned antibiotics. In this subgroup of patients, their RRF and daily urine volume showed significant reduction at day 14 and returned to near baseline values at day 42. The degree of reduction in RRF and urine volume did not differ significantly between the patients treated with cefazolin plus netilmicin and cefazolin plus ceftazidime.

Conclusion. Intraperitoneal cefazolin plus netilmicin and cefazolin plus ceftazidime have similar efficacy as empirical treatment for CAPD peritonitis. In CAPD patients with RRF, significant but reversible reduction in RRF and 24-hour urine volume could occur after an episode of peritonitis, despite successful treatment by i.p. antibiotics. The effect of i.p. cefazolin plus netilmicin, or i.p. cefazolin plus ceftazidime on RRF in CAPD patients with peritonitis does not appear to be different. Our findings do not support the routine use of cefazolin and ceftazidime as the empirical treatment for CAPD peritonitis.

Key words: continuous ambulatory peritoneal dialysis, peritonitis, residual renal function, antibiotic, aminoglycosides.

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In recent years, it has been recognized that preservation of residual renal function (RRF) in patients undergoing continuous ambulatory peritoneal dialysis (CAPD) is associated with improved survival and better quality of life [1, 2]. The factors that influence the rate of loss of RRF in CAPD patients have not been completely elucidated. It has been suggested that higher rate of peritonitis, the presence of diabetes mellitus, and obesity are associated with a more rapid loss of RRF [3–5]. It has also been reported that CAPD patients who have been treated with aminoglycosides have a faster rate of decline of RRF [4, 6]. In view of the potential nephrotoxic effect of aminoglycosides, the International Society for Peritoneal Dialysis (ISPD) guidelines for the treatment of CAPD peritonitis 2000 recommended that a first and a third generation cephalosporin, such as cefazolin plus ceftazidime, be used as the initial empirical antibiotic treatment for CAPD-related peritonitis, and that the conventional regimen of cefazolin plus netilmicin be avoided in patients with RRF [7].

However, it should be noted that the clinical efficacy of cefazolin plus ceftazidime for the treatment of CAPD peritonitis has not been compared with cefazolin plus netilmicin in prospective randomized clinical trials. There is also a lack of prospective data regarding the effect of a single episode of peritonitis and the use of intraperitoneal (i.p.) aminoglycosides on RRF in CAPD patients.

The aim of this study was to compare i.p. cefazolin plus netilmicin versus i.p. cefazolin plus ceftazidime for the treatment of CAPD peritonitis in terms of their clinical efficacy and their effect on RRF.

METHODS

Study design

This study was a prospective, randomized, open-labeled study in stable CAPD patients in a single dialysis

center of a university teaching hospital. The randomization was done by computer generated randomization table. The study protocol was approved by the Hospital Ethical Committee for Clinical Research.

Subjects

All stable CAPD patients aged 18 or older in the dialysis center who had developed clinical evidence of peritonitis were eligible for the study. Peritonitis was diagnosed when abdominal pain and cloudy peritoneal dialysis fluid (PDF) occurred with or without fever, and when peritoneal white cell count (WBC) count was >100/mm^3 with >50% neutrophils. Informed consent was obtained from each patient. The flow of patients in the study is shown in Figure 1.

Exclusion criteria

Patients who had known hypersensitivity to cephalosporins or aminoglycosides, suspected fungal or tuberculous peritonitis and relapsing peritonitis (i.e., an episode of peritonitis within 4 weeks after apparent recovery and cessation of antibiotics from a previous episode of peritonitis), and active exit site infection were excluded from the study.

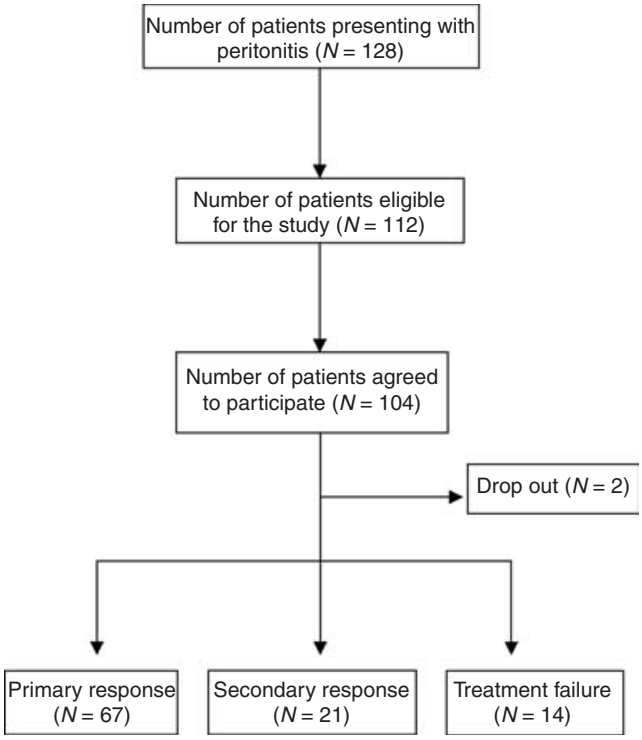

Fig. 1. Flow of patients in the study.

Definitions

Cure is defined as complete resolution of signs and symptoms of peritonitis with negative PDF cultures and no further episodes of peritonitis within 28 days following the cessation of antibiotic treatment. Primary cure refers to cure by the assigned i.p. antibiotics. Primary treatment failure is defined as the presence of fever, abdominal pain, and turbid peritoneal dialysate, and if the total peritoneal WBC counts is >50% of the pretreatment values after 3 days of treatment by the assigned antibiotics. Secondary cure refers to cure after adjustment of antibiotics or changing to second line antibiotics in patients with primary treatment failure. Secondary treatment failure is defined as treatment failure despite adjustment of antibiotics or changing to second line antibiotics for 3 to 5 days in patients with primary treatment failure. Relapse is defined as recurrence of peritonitis with the same microorganism within 28 days of clearing of the initial peritonitis episode and cessation of antibiotic therapy.

Treatment regimen

Patients who fulfilled the entry criteria were randomized to receive either i.p. cefazolin plus netilmicin or i.p. cefazolin plus ceftazidime, given once daily in the long dwell. The dosage of the i.p. antibiotics were as follows: cefazolin (1 g per 2 L PDF); netilmicin (0.6 mg/kg body weight per 2 L PDF); and ceftazidime (1 g per 2 L PDF). The duration of treatment was 14 days. If the peritonitis failed to respond to the assigned i.p. antibiotics by day 3 (primary treatment failure), the antibiotics would be adjusted according to the PDF bacterial culture results or be changed to second line antibiotics (vancomycin plus amikacin) if the PDF bacterial cultures were negative. Removal of the peritoneal dialysis catheters would be considered in patients with primary treatment failure whose peritonitis failed to improve after adjusting the i.p. antibiotic regimens for 3 to 5 days (secondary treatment failure).

Monitoring

The duration of follow-up was 42 days. Before starting treatment and at days 1, 3, 5, 7, 10, 14, 28 after the initiation of treatment, peritoneal fluid total plus differential WBC count were measured. At days 0, 3, 7, 10, 14, and 28 after the initiation of treatment, bacterial and fungal cultures of fresh peritoneal effluent were performed. Complete blood count, liver and renal function tests were measured before and at 14 and 42 days after the initiation of treatment.

Measurement of RRF

For patients with RRF of greater than 1 mL/min as determined at the last routine follow-up before entry into the study, their RRF and daily urine output were determined at days 1, 14, and 42 after entry into study. Estimated RRF was calculated as the mean of creatinine