Peritonitis during Continuous Ambulatory Peritoneal Dialysis

Treatment with Pefloxacin: First Results and Pharmacokinetics

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Dear Sir,

The broad spectrum of the new quinolones in general and of pefloxacin in particular [1] demonstrates an activity not only against the majority of gram-negative bacilli, but also against gram-positive cocci, particularly against species of methicillin-sensitive or -resistant *Staphylococcus*. These features have led us to use pefloxacin as first-line treatment of peritonitis in patients on continuous ambulatory peritoneal dialysis and to study its pharmacokinetics.

Pefloxacin cannot be used via the intraperitoneal route, as it precipitates in contact with concentrated saline solutions. Intravenous antibiotic treatment with pefloxacin as monotherapy was administered in 15 cases of peritonitis occurring in patients aged between 22 and 77 years (mean age 46 years) on continuous ambulatory peritoneal dialysis by means of 1-hour infusions once every 24 h at a dose of 800 mg on the 1st day, then 400 mg on the following days with transfer to oral treatment at the same dosage as soon as possible (after the 3rd day). The treatments were continued for 13 days.

The antibiotic concentrations were determined by a microbiological technique using the Difco Antibiotic Medium No. 1 (pH 6.6) and a test strain of *Escherichia coli*. The samples and their dilutions in fetal serum, in the case of serum samples, in dialysis fluid, in the case of dialysate, and standard range were deposited in a volume of 25 µg on paper disks (Schleicher and Schnell No. 740-2). Each assay was performed in triplicate. The limit of detection was close to 0.09 mg/l.

Out of the 15 cases with peritonitis, the bacteria responsible were isolated in 11 cases, with the isolation of a total of 12 organisms: *Staphylococcus aureus* (n = 4), *Staphylococcus epidermidis* (n = 4), *Streptococcus mitis* (n = 1), *Streptococcus sanguis* (n = 1), *Streptococcus bovis* (n = 1), and *Acinetobacter calcoaceticus* (n = 1).

Only two strains, *S. bovis* (minimal inhibitory concentration 32 mg/l) and *S. sanguis* (minimal inhibitory concentration 16 mg/l), were resistant to pefloxacin, and treatment was suspended immediately. The other strains were all sensitive; the minimal inhibitory concentrations were between 0.12 and 0.5 mg/l for the *Staphylococci* and 1 mg/l for *A. calcoaceticus*.

Pharmacological results are shown in table I. The concentrations in the residual dialysis bags represented 50.8% of the serum level at the end of the first infusion

Table I. Pefloxacin concentrations (mg/l) in the serum and the dialysis bags according to the dosage and the stage of the peritonitis

Mean Serum level

Peak	11.2 ± 2.5	9.96 ± 2.18	5.57 ± 1.17	8.17 ± 1.88		
(15)	(15)	(6)	(3)	Residual	5.48 ± 1.62	4.74 ± 1.5
	(15)	(15)	(7)	(3)		2.57 ± 0.96
						5.47 ± 2.43

Mean bag level

Peak	5.7 ± 1.8	4.97 ± 1.61	2.93 ± 0.36	7.2 ± 2.7	
(15)	(13)	(3)	(2)		
Residual		4.55 ± 1.59	3.69 ± 1.25	2.41 ± 1.51	5.77 ± 3.58
(15)	(15)	(7)	(3)		

Number of assays in parentheses.

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compared with 83% of the residual level, i.e., a mean of 58.9% of the serum levels on the 3rd day compared with 65.6% on the 14th day which demonstrates that the reduction in the inflammatory condition of the peritoneum does not interfere with the diffusion of the antibiotic in the blood-dialysis fluid direction. The serum half-life varied between 17 and 21 h (11 h in patients with normal renal function) [2]. Cure was obtained in 11 out of 15 cases with peritonitis. Failure was due to resistant strains in 2 cases (*S. bovis* and *S. sanguis*) and in 1 case to an initially sensitive strain of *S. epidermidis* (minimal inhibitory concentration 0.5 mg/l) which became resistant (minimal inhibitory concentration 8 mg/l) on the 7th day of treatment. The 4th failure represented a case of *S. aureus* peritonitis (minimal inhibitory concentration 0.25 mg/l) with contamination of the catheter. Side effects were observed in 5 of the 15 patients; the treatment was not suspended, but the dosage reduced from 400 to 200 mg. These side effects consisted of bone pain (2 patients), nausea (2 patients), vertigo (2 patients), or gastrointestinal disturbances (1 patient). All patients presenting these side effects had serum peak levels between 11 and 18 mg/l. The concentrations obtained in the dialysis bags by oral or intravenous administration (57–58% of the serum levels) were high and very similar to the concentrations obtained in the cerebrospinal fluid [1]. The diffusion is minimally influenced by the inflammatory state of the peritoneum.

The new quinolones should, therefore, find a place in the treatment of peritonitis in patients on continuous ambulatory peritoneal dialysis, but they must be associated with another antibiotic, e.g., cephaioin, in order to prevent the development of resistance during treatment and to widen the spectrum to certain bacteria occasionally responsible for peritonitis which are poorly sensitive to these products (streptococci, for example, which are responsible for about 10% of peritonitis cases during continuous ambulatory peritoneal dialysis).

References

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