CEPHALOTIN CONCENTRATION DURING HAEMO- AND PERITONEAL DIALYSIS

A. TOURKANTONIS, G. MÖSSNER, K. A. EGETMEYER and V. HEINZE

Medical Policlinic and Medical Clinic, University of Freiburg i. Br.,
Freiburg i. Br., Federal Republic of Germany

According to Kabins and Cohen (1964), Kunin and Atuk (1966), as well as Tourkantonis et al. (1967) the antibiotic cephalotin shows remarkable advantages in the treatment of renal-insufficient patients: maximum renal tissue and urine levels, few side effects, no nephrotoxicity, low toxicity despite cumulation in impaired kidney function, and applicability in case of penicillin allergy. The molecular weight and extent of protein binding of cephalotin led us to expect that the substance will be eliminated by dialysis procedures. The dialysis-induced elimination rate must be taken into consideration in selecting the dose of the antibiotic. We have therefore followed the serum concentration of cephalotin during extracorporeal haemodialysis and peritoneal dialysis and estimated its elimination rate and half-life period.

METHODS

Haemodialysis: the cephalotin determinations were performed in 7 male and 3 female patients with terminal chronic uraemia (Ccr 0–2 ml/min./1.73 m²); 5 dialyses each were carried out with the Kiil-Scribner dialyzer (blood flow 150–200 ml/min.) and the Travenol twin coil PS 145 in the compact kidney system (fluid rate 200–250 ml/min.). Duration of dialysis: 10 hours. At the beginning of dialysis 1000 mg of cephalotin were injected intravenously and after 0.5, 1, 2, 4, 6, 8 and 10 hours blood samples were taken from the extracorporeal blood for determination of cephalotin concentration.

For peritoneal dialysis we applied the following technique: initial instillation of 21 dialysis fluid in the abdominal cavity, immediately following drainage of 1 l and consecutive infusion of the next litre of fresh fluid and so on. The perfusion volume per dialysis is 70 l by an average period of 16 hours.

In 2 male and 2 female patients with terminal chronic uraemia (Ccr 0–4 ml/min./1.73 m²), who were treated by a combination of strict low protein ‘potato-egg diet’ and once weekly peritoneal dialysis, we carried out cephalotin estimations. Two patients received 1000 mg of cephalotin intravenously after start of peritoneal dialysis. After 0.5, 1, 2, 4, 8 and 12 hours the antibiotic concentrations were determined in the venous blood flow. In addition, we determined the elimination rate of cephalotin in the first and in the second 20 l of dialysate.

In the case of the other 2 patients 14.2 mg/l and 28.4 mg/l, respectively, of cephalotin were added to dialysis fluid. Subsequently, we traced the cephalotin concentrations in the blood 1, 4, 8 and 12 hours after the beginning of dialysis and we again determined the cephalotin amount in the first and in the second 20 l of dialysate.

The cephalotin concentration was determined in accordance with the agar-diffusion test (cup-plate method, modified according to Klein (1957)), elimination coefficient and half-life time were calculated in conformity with the methods of Dost (1953).
RESULTS

Haemodialysis: the cephalotin concentration amounted to 84.0 and 2.2 mcg%, 0.5 and 10 hours, respectively, after the beginning of dialysis with the Kil dialyzer, the elimination coefficient was 0.256 and the half-life time on average 2.7 hours. For the twin coil PS 145 we found the following values: cephalotin concentration 51.0 and 1.3 mcg/ml, 0.5 and 10 hours after the beginning of dialysis, elimination coefficient 0.280 and half-life time of 2.5 (Table I) hours on average. Figures 1 and 2 show that the cephalotin concentration descends exponentially and was already reduced approximately to one-half 2 hours after the beginning of dialysis.

TABLE I

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<th>1</th>
<th>2</th>
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<th>6</th>
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Peritoneal dialysis

Following a single intravenous injection of 1000 mg of cephalotin 0.5 and 10 hours after the beginning of peritoneal dialysis, cephalotin concentrations of 39.6 and 3.2 mcg/ml, respectively, were estimated. The half-life time amounted to 3.8 hours (Fig. 3). With the first 201 of the perfusate 57.8–80.8 mcg/ml were eliminated, with the second 201, 6.8–27.0. Maximum concentration in the dialysate was 2.7–5.4 mcg/ml.

Following addition of 14.2 and 28.4 mg of cephalotin/l to the perfusate, the serum concentrations were 0.47 mcg/ml and 0.99 mcg/ml, respectively, 1 hour after the beginning of dialysis (Fig. 3). After 12 hours the corresponding values amounted to 2.32 mcg/ml and 3.35 mcg/ml. In the first 201 of perfusate the cephalotin concentrations were 12 mcg/ml and 22 mcg/ml, in the second period 3.5 and 12.0 mcg/ml, respectively.

CONCLUSIONS

1. The cephalotin concentrations in serum are lowered by extracorporeal haemodialysis and to a smaller degree also by peritoneal dialysis. The elimination quotient was 28% for the Kil-Scribner dialyzer as well as the Travenol twin coil PS 145.

2. The cephalotin half-life time in haemodialyzed patients was 3 to 4 times longer after single application than in normal persons; it amounted to only one-half of the value in comparison with non-dialyzed chronic uraemics. Cephalotin-treated patients should therefore
Fig. 1. Decrease of the cephalotin concentration in serum in 5 extracorporeal haemodialyses with the Travenol twin coil PS 145.
--- Average decrease.

Fig. 2. Decrease of the cephalotin concentration in serum in 5 extracorporeal haemodialyses with the Kill dialyzer.
--- Average decrease.
receive a dose of the antibiotic at intervals of 2–3 hours during an extracorporeal haemodialysis.

3. After a single intravenous injection of 1000 mg of cephalotin concentrations of 5.7 mcg/ml were reached in the peritoneal dialysate indicating a mean antibacterial level. In consideration of the half-life time of the antibiotic, cephalotin-treated patients under peritoneal dialysis should receive a single dose of cephalotin every 6 hours.

Fig. 3a. Serum levels and total amount of cephalotin eliminated in dialysate after single intravenous injections of 1000 mg during 2 peritoneal dialyses.

- □ Average decrease.
- ■ Total amount eliminated.

Fig. 3b. Serum levels as well as concentration and total amount of cephalotin eliminated in dialysate during peritoneal dialysis.

- ■ After addition of 28.4 mg/l perfusate.
- — — □ After addition of 14.2 mg/l perfusate.
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4. After adding 28.4 mg of cephalotin per litre of peritoneal dialysis fluid, the serum concentration of the antibiotic reaches 3.3 mcg/ml. This level is sufficient for the prophylaxis and treatment of common infections by sensitive organisms.

REFERENCES