ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Dec. 1983, p. 955-956
0066-4804/83/120955-02$02.00/0

Vol. 24, No. 6

Comparison of the Concentrations of Ceftazidime in the Serum of Newborn Infants After Intravenous and Intramuscular Administration

A. BOCCAZZI,[1]* M. RIZZO,[2] M. L. CACCAMO,[2] AND B. M. ASSAEL[1]

Second Department of Pediatrics[1] and Newborn Unit,[2] University of Milan Medical School, Milan, Italy

Received 21 March 1983/Accepted 27 September 1983

The concentrations of ceftazidime in serum were studied in 16 preterm and term neonates to whom a single dose of 50 mg/kg had been administered intramuscularly or intravenously. After intramuscular injection, concentrations of ceftazidime in serum were comparable to those obtained with the intravenous dose, although they were more variable. Peak serum levels ranging from 50 to 102 μg/ml were reached 30 to 60 min after intramuscular injection. The concentrations declined monoexponentially after the peak, with a mean half-life of 3.8 ± 1.1 h. Concentrations of ceftazidime in serum declined biexponentially after intravenous injection, with a terminal half-life of 4.7 ± 1.5 h.

Ceftazidime (CAZ), a beta-lactam antibiotic with an expanded spectrum of in vitro activity that includes gram-negative pathogens (5, 6), has a potential for use in the treatment of neonatal infections. The study described in this report was designed to obtain preliminary pharmacokinetic data during the neonatal period.

A single dose of 50 mg of CAZ per kg was administered to 16 neonates with suspected or diagnosed sepsis, after which a standard antibiotic regimen was administered. Informed oral consent was obtained from parents before administration of CAZ.

CAZ was administered intravenously (i.v.) to seven patients at a gestational age of 32 to 40 weeks (mean age, 34.8 weeks), a birth weight of 1,140 to 3,500 g (mean weight, 2,470 g), and a postnatal age of 1 to 9 days (mean age, 6 days). CAZ was administered intramuscularly (i.m.) to nine neonates at a gestational age of 34 to 48 weeks (mean age, 36.8 weeks), a birth weight of 1,480 to 3,900 g (mean weight, 2,860 g), and a postnatal age of 1 to 15 days (mean age, 8 days).

The CAZ used in this study was provided in 250-mg vials by Glaxo S.P.A., Verona, Italy. The contents of the vial were dissolved in 1 ml of sterile water, and the appropriate dosage per kilogram of body weight was administered i.m. or further diluted to a concentration of 50 mg/ml for i.v. infusion over 5 min into a peripheral vein.

Blood samples (0.2 ml) obtained at 15, 30, and 60 min and at 3 and 12 h by heel puncture were centrifuged within 2 h. The serum so obtained was stored at −20°C and assayed within 1 week. Concentrations of CAZ in serum were measured by an agar disk diffusion method (7), using *Morganella morganii* 557/CR as the test organism. The minimal concentration of CAZ detectable with this assay was 0.062 μg/ml.

The mean concentrations (± standard deviation) of CAZ in the two groups of neonates are shown in Table 1. Concentrations of CAZ after i.v. injection declined biexponentially. The postdistributive phase occurred 30 to 60 min after administration. Individual profiles of serum concentrations versus time were fitted by means of a nonlinear computer program analysis (4). The half-life of the terminal (elimination) phase (Table 1) was calculated from the following equation: $t_{1/2} = 0.693/\beta$, where β is the slope of the terminal phase. Peak serum concentrations of CAZ ranging between 54 and 102 μg/ml were reached within 0.5 to 1 h after i.m. injection. Concentrations of CAZ 15 min after i.m. injection were significantly lower than corresponding levels after i.v. injection. After absorption, CAZ concentrations declined monoexponentially. The slope (β) of the declining phases was calculated from the regression analysis of the log concentrations versus time from the peak time to 12 h (6 h in one case).

The elimination half-life ($t_{1/2}$) was given by $0.693/\beta$. The elimination half-lives of CAZ after i.v. and i.m. injections were slightly different, but such differences did not reach a statistical significance ($P > 0.05$ by the two-tailed Student's t test).

The results presented in this study show that a dose of 50 mg of CAZ per kg allows elevated serum concentrations of the antibiotic to be reached in neonates. Since the 90% minimal

TABLE 1. Mean serum concentrations of ceftazidime and half-lives after administration of a single dose of 50 mg/kg

Time after drug administration	Mean drug concn (μg/ml)[a]	
	i.v. injection (7 neonates)	i.m. injection (9 neonates)
15 min	109.3[b] ± 19.9	53.0[b] ± 22.4
30 min	85.4 ± 11.4	67.2 ± 24.0
60 min	64.0 ± 9.0	68.2 ± 19.3
3 h	48.1 ± 8.3	42.1 ± 14.1
6 h	25.6 ± 7.7	23.7 ± 8.5
12 h	11.8 ± 4.1	8.9 ± 5.6

[a] The half-lives of the terminal (elimination) phase were 4.7 ± 1.5 h for i.v. injection and 3.8 ± 1.1 h for i.m. injection.

[b] $P < 0.001$ by Student's t test.

inhibitory concentrations of most pathogens sensitive to CAZ are lower than 8 μg/ml (1–3), therapeutically active concentrations of the drug are maintained for many hours with this dosage. This can be achieved by administering the antibiotic either i.v. or i.m.

This work was supported in part by a grant from Glaxo S.P.A., Italy.

LITERATURE CITED

1. **Brumfitt, W., and J. M. T. Hamilton-Miller.** 1981. The susceptibility of nosocomial pathogens to ceftazidime. J. Antimicrob. Chemother. 8(Suppl. B):15–21.
2. **Harper, P. B.** 1981. The in vitro properties of ceftazidime. J. Antimicrob. Chemother. 8(Suppl. B):5–13.
3. **Leigh, D. A., and D. Nisbet.** 1981. Antibacterial activity of ceftazidime (GR 20263) against routine hospital isolates and highly resistant strains of *Enterobacteriaceae* and *Pseudomonas aeruginosa*. J. Antimicrob. Chemother. 8(Suppl. B):107–110.
4. **Metzler, C. M.** 1979. NonLin, a computer program for parameter estimation in nonlinear situations. Technical report 7292/7292/005. The Upjohn Co., Kalamazoo, Mich.
5. **Neu, H. C., and P. Labthavikul.** 1982. Antibacterial activity and β-lactamase stability of ceftazidime, an aminothiazolyl cephalosporin potentially active against *Pseudomonas aeruginosa*. Antimicrob. Agents Chemother. 21:11–18.
6. **Phillips, I., C. Warren, K. Shannon, A. King, and D. Hanslo.** 1981. Ceftazidime: in vitro antibacterial activity and susceptibility to beta-lactamases compared with that of cefotaxime, moxalactam and other beta-lactam antibiotics. J. Antimicrob. Chemother. 8(Suppl. B):23–31.
7. **Thornton, J. E.** 1981. The microbiological assay of ceftazidime. J. Antimicrob. Chemother. 8(Suppl B):225–226.