CIPROFLOXACIN PHARMACOKINETICS IN SUBJECTS WITH NORMAL AND IMPAIRED RENAL FUNCTION

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The antibacterial spectrum of ciprofloxacin suggests it may be of value in treating urinary tract infections (UTI). We therefore studied its pharmacokinetics in healthy volunteers and patients with renal impairment to establish dosage guidelines. Local ethical committee approval and fully informed consent were obtained.

24 subjects, weighing 68±14 kg were equally divided into four groups according to creatinine clearance (Clcr) - group I >80, group II 31-80, group III 10-30, group IV <10 $ml.min^{-1}$ 1.73 m^{-2}. Following collection of baseline samples of plasma and urine, 100 mg ciprofloxacin was injected intravenously over 5 min. Plasma samples were collected at 0.5, 1, 1.5, 2, 4, 6, 8, 12 and 24 h and also at 48 h for groups III and IV. Urine samples were collected over 0-2, 2-4, 4-6, 6-8, 8-12, 12-24, 24-48 h and also over 48-72 h for groups III and IV. Ciprofloxacin was assayed by HPLC (Wingender et al., 1984). Plasma clearance (Clp) and distribution volume (Vd) were calculated on a two compartment open model. Renal clearance (Clr) was calculated by the standard method and non-renal clearance (Clnr) from:- Clnr = Clp-Clr. Correlations between Vd and body weight were by linear regression, correlations between Clp, Clr and Clcr were by Spearman's rank analysis.

Vd, which was related to ideal body weight (IBW) ($r=0.74$ $p<0.001$) but not to actual body weight (ABW), was 2.2±0.6 $l.kg^{-1}$ of IBW. Clcr correlated with both Clp ($r_s=0.50$ $n=24$ $p<0.02$) and Clr ($r_s=0.93$ $n=24$ $p<0.001$). In group I 57±9% of the drug was eliminated renally and 43% non-renally. Clr was approximately 3xClcr in group I, 2.5xClcr in group II, 1.5xClcr in group III and approximately equal to Clcr in group IV (see table). Clnr, which was not related to age, sex, IBW, ABW or Clcr, was 238±97 $ml.min^{-1}$. In healthy volunteers 30-43% of the drug was recovered from the urine as metabolites (Höffken et al., 1985).

Group	Clcr	Clr	Clp	
	$ml.min^{-1}$	$ml.min^{-1}$	$ml.min^{-1}$	%
I	100	300	538	100
II	50	125	363	67
III	30	45	283	53
III	10	15	253	47
IV	0	0	238	44

For establishing therapeutic guidelines Clp was calculated from:

mean Clnr (238 $ml.min^{-1}$) + Clr,

for the values of Clcr shown in the table.

The ciprofloxacin MIC for common pathogens in urine is 2 $mg.l^{-1}$ (Reeves et al., 1984). This level was exceeded for over 12 h in groups I and II, for 10±3 h in group III and for 7±4 h in group IV. Subject to the efficacy and toxicity of ciprofloxacin with chronic dosing, we suggest that for UTI 100 mg tds should be given to patients with a Clcr <30 $ml.min^{-1}$, and 200 mg bd to patients with a Clcr of 30-50 $ml.min^{-1}$, instead of the usual dose of 250 mg bd.

Wingender, W. et al. (1984). Eur. J. Clin. Microbiol. 3: 355-359.
Reeves, D.S. et al. (1984). J. Antimicrob. Chemother. 13: 333-346.
Höffken, G. et al. (1985). Antimicrob. Ag. Chemother. 27: 375-379.