EPITHEORESE KLINIKES FARMAKOLOGIAS
KAI FARMAKOKINETIKES, INTERNATIONAL
EDITION 16: 28-29 (2002)

Pharmacokinetics of Oral Sparfloxacin, 400 mg Single Dose, in Healthy Young and Elderly Volunteers

A. Tsona, P. Nikolaidis., E. Koumentaki, P. Kollaras, S. Metallidis and A. Turkantonis

Infectious Disease Division, First Department of Internal Medicine, University Hospital o AHEPA, Thessaloniki, Greece

S u m m a r y. The pharmacokinetics of oral sparfloxacin following a single 400 mg oral dose were evaluated in elderly volunteers (mean age 73 years) and young volunteers (mean age 30 years). There were no significant differences in serum T_{MAX} and C_{MAX}, but there was a slight increase to serum AUC and $T_{1/2}$ in elderly volunteers. The serum AUC value in elderly was 43.3±10.2 mg·h/l versus 28.05±8.6 mg·h/l in young volunteers and the $T_{1/2}$ value in elderly was 33.3±8.8 h versus 18.6±1.8 h in young volunteers.

INTRODUCTION-AIM

Sparfloxacin is a new quinolone with broad antibacterial activity. It is more active than ciprofloxacin against staphylococci, streptococci and enterococci. Sparfloxacin is more active than ciprofloxacin against isolates in the Bacteroides fragilis group and against clostridia. On the other hand, sparfloxacin is less active than ciprofloxacin against members of the family Enterobacteriaceae or against Pseudomonas aeruginosa (1,2,3,4). Its pharmacokinetic properties include a long serum half life ranged from 16 to 22h and a weak plasma protein binding (45-46%). Sparfloxacin is eliminated by renal and non-renal processes including biliary excretion and probably transinstestinal secretion(5). In the present study the pharmacokinetic parameters in elderly volunteers were compared with those in young volunteers.

MATERIALS AND METHODS

Fourteen healthy volunteers were included in the study. They given written consent to participate after the aim of the study was explained tc them. All volunteers were healthy and their standard hematological and biochemical parameters were normal prior to the study. The volunteers were divided into two groups on the basis of thei age. Group 1 included seven young healthy volunteers and Group 2 included seven elderly healthy volunteers. The demographic characteristics of the subjects are shown in Table 1.

Table 1.
Mean demographic data for subjects in this study

Parameter	*Mean ± SD for GROUP 1*[a]	*Mean ± SD for GROUP 2*[a]
Age (yr)	30 ± 6 (22-40)	73 ± 3 (70-78)
Gender, M/F[b]	2/5	4/3
Weight (kg)	70 ± 15 (55-105)	70 ± 3 (66-75)
CLcr (ml/min)[c]	97 ± 21	61 ± 4
Creatinine (mg/l)	1.01 ± 0.12	0.99 ± 0.08

[a] Ranges are indicated in parentheses
[b] M, male; F, female
[c] Estimated by equation of Cockroft

The unit dose of sparfloxacin was 400 mg given by mouth. Serum specimens were obtaine by multiple venuspuncture. Specimens wer taken at time 0, 0.5, 1, 1.5, 2, 2,5, 3, 4, 8, 12, 24 48, 72 h after dosing and were stored at –20 ^{0} C until analysis by HPLC (high-performance liqui chromatographic). Pharmacokinetic analyse were performed according to a two-compartmen model. Statistical analysis was performed usin mean (± S.D.) values and the t-test, in whic $P<0.05$ was taken as statistically significant.

RESULTS

Mean levels of sparfloxacin in serum after a single oral dose of 400 mg, from healthy young and healthy elderly volunteers are illustrated in Figure 1. The pharmacokinetic parameters that were determined were the peak plasma concentration (Cmax), the time to Cmax (Tmax), the area under the plasma concentration-time curve (AUC), elimination rate constant (K), the plasma elimination half life ($T_{1/2}$) and the total body clearance (Cl_t). Mean pharmacokinetic parameters are provided in Table 2.

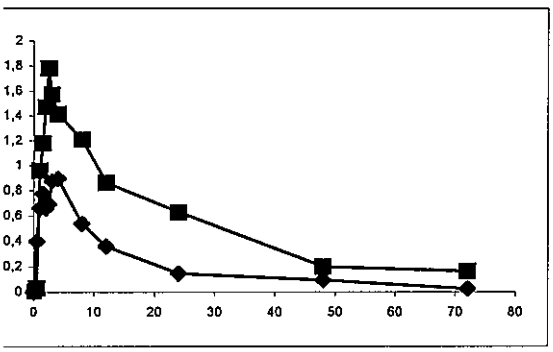

Figure 1. Serum concentration of sparfloxacin (mg/L) in young and elderly volunteers after dose of 400mg per os. -◆-: young; -■-: elderly

Table 2
Comparison of pharmacokinetic parameters of sparfloxacin following oral administration of 400 mg of sparfloxacin[a] in healthy young and healthy elderly volunteers

	C_{max} mg/l	T_{max} h	AUC_{0-96} mg·h/l	AUC_{0-00} mg·h/l	K h^{-1}	$T_{1/2}$ h	Cl_t[b] ml/min
Group 1 (n=7)	1.46 ± 0.35	3.2 ± 2.4	26.96 ± 8.4	28.05 ± 8.6	0.037 ± 0.003	18.6 ± 1.8	258.9 ± 86.0
Group 2 (n=7)	1.71 ± 0.87	3.3 ± 2.2	38.5 ± 11.5	43.3 ± 10.2	0.021 ± 0.005	33.3 ± 8.8	171.5 ± 67.1

[a] Parameters given are mean values ± standard deviations

[b] Cl_t, total body clearance

CONCLUSIONS

A comparison of the pharmacokinetic parameters in the young and the elderly volunteers justifies several conclusions. There were no significant differences between young and elderly subjects in Tmax and Cmax values, indicating that there is no delay in the absorption of sparfloxacin in the elderly. Significant increases in $T_{1/2}$ and AUC values were observed in elderly compared with young volunteers. These differences most probably reflect the decrease of the total body clearance in the elderly (171.5 ml/min in the elderly versus 258.9 ml/min in the young). The decrease of the total body clearance was ascribed to the reduction of the renal function in the elderly. Despite of the normal serum creatinine, the clearance of creatinine in elderly was significant decreased (61.2 ml/min) compared to the young's clearance of creatinine (97.1 ml/min).Therefore, there is no pharmacokinetic rationale for modifying the recommended sparfloxacin dosage regimen according to the age of the patient. The pharmacokinetic of sparfloxacin is not affected by the patient age but by the possible existence of renal failure and the recommended dosage of sparfloxacin remains 400 mg once a day.[6,7]

Acknowledgments: We wish to thank Bayer for invaluable advice and assistance and for the supply of sparfloxacin tablets used in this study.

REFERENCES

1. Barry A.L., Fuchs P.C.: In vitro activities of sparfloxacin, tosufloxacin, ciprofloxacin and fleroxacin. *Antimicrob. Agents Chemother. 35*: 955-960 (1991)
2. Kojima T., et al.: In vitro activity of AT-4140 against clinical bacterial isolates. Antimicrob. *Agents Chemother. 33*: 1980-1988 (1990)
3. Kojima T., et al.: In vitro activity of AT-4140 against quinolone- and methicillin-resistant Staphylococcus aureus. Antimicrob. *Agents Chemother. 34*: 1123-1127 (1990)
4. Nakamura S., et al.: In vitro and in vivo antibacterial activities of AT-4140, a new broad-spectrum quinolone. Antimicrob. *Agents Chemother. 33*: 1167-1173 (1989)
5. Montay G.: Pharmacokinetics of sparfloxacin in healthy volunteers and patients: a review. *J. Antimicrob. Chemoth. 37*: 27-39 (1996)
6. Montay G., et al.: Pharmacokinetics of sparfloxacin in humans after single oral administration at doses of 200-800 mg. *J. Clin. Pharmacol. 34*: 1071-1076 (1994)
7. Shimada J. et al. Clinical pharmacokinetics of sparfloxacin. *Clin. Pharmacokinet. 25*: 358-369 (1993)