Pharmacokinetics of Levofloxacin in Healthy Thai Male Volunteers

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Abstract

The pharmacokinetics of levofloxacin, a new fluoroquinolone, were investigated in 12 healthy Thai male volunteers with an average age (SD) of 22.92 (2.50) years. A single oral dose of 300 mg or 500 mg levofloxacin was given to subjects following an 8- hour overnight fast. The drug was given in a controlled, randomized, 2 x 2 crossover design with a 1 week washout period. Venous blood samples were drawn prior to and from 0.25 up to 48 hours after dosing. Plasma levofloxacin concentrations were determined by HPLC assay.

The pharmacokinetics of levofloxacin were well described by a linear, 2-compartment open model with first-order absorption with lag time and first-order elimination. Mean ± SEM of C_{max} after 300 mg and 500 mg dose was 4.83 ± 0.33 and 7.75 ± 0.71 μg/mL, respectively. T_{max} ranged from 0.7 to 0.8 hours for both doses. Mean ± SEM of $AUC_{0-\infty}$ was 35.77 ± 2.06 μg x h/mL for 300 mg dose and 61.57 ± 2.84 μg x h/mL for 500 mg dose. High distribution with V_{ss}/F value of approximately 1.5 L/kg was demonstrated after both doses. Mean ± SEM of CL/F value was 8.64 ± 0.41 L/h and 8.31 ± 0.37 L/h for a 300-mg and a 500-mg dose, respectively. Long $t_{1/2\beta}$ of 7 to 8 hours with the mean residence time of 10.43 ± 0.43 hours and 10.49 ± 0.38 hours after 300 mg and 500 mg dose, respectively, was observed. The results suggested that an oral 300 mg dose once daily provides sufficient C_{max} to cover most Gram-negative and atypical bacteria (median MIC_{90} 0.032-0.5 μg/mL) common in mild to moderate respiratory tract infections or complicated urinary tract infections and Gram-positive bacteria (median MIC_{90} 0.5 μg/mL) common in skin and soft tissue infections. For severe cases or *Streptococcus pneumoniae* (MIC_{90} 2 μg/mL) infection, a 500-mg dose should be recommended.

Key word : Levofloxacin, Pharmacokinetics, Fluoroquinolone

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Levofloxacin or L-ofloxacin is a new fluoroquinolone which is an optically active isomer [(S)-(-)-isomer] of ofloxacin. This drug has been shown to be active *in vitro* against aerobic Gram-positive and Gram-negative bacteria and certain types of pathogens, such as *Mycoplasma, Chlamydia, Legionella* and *Mycobacteria* spp[1-3]. It has been approved by the US Food and Drug Administration for the treatment of mild to moderate acute maxillary sinusitis, acute exacerbation of chronic bronchitis (AECB), community-acquired pneumonia (CAP), uncomplicated skin and soft tissue infections (SSTIs) in the dose of 500 mg once daily for 7-14 days. It is also recommended for the treatment of complicated urinary tract infections (UTIs), including acute pyelonephritis in the dose of 250 mg once daily for 10 consecutive days. In Europe, levofloxacin is recommended for similar indications but the dose recommended varies in some conditions, e.g. for AECB it can be 250-500 mg once daily, for CAP 500 mg once or twice daily, and for SSTIs 250 mg once or 500 mg once or twice daily[4].

In Thailand, this drug has already been launched with the recommended dose of 300 mg administered orally every 24 hours for 7-14 days for the above indications. This dose is different from that recommended in the US or in Europe but similar to the total daily dose recommended in Japan (100 mg three times daily). The present study was thus designed to investigate the pharmacokinetics of levofloxacin orally administered in a single dose of 300 and 500 mg in healthy Thai male volunteers. The results obtained may provide a guideline for the appropriate dose in Thai patients for certain infections.

SUBJECTS AND METHOD

Subjects

Twelve Thai male volunteers aged between 20 and 30 years were enrolled into the study. All volunteers were determined to be healthy on the basis of medical history, physical examination, hematological and biochemical investigations including liver function test, blood urea nitrogen and serum creatinine determination and urinalysis. None had a history of quinolone or fluoroquinolone allergy. No other medications including vitamins were allowed within 2 weeks prior to and during the study. No subject drank alcohol or smoked. Strenuous physical activity was prohibited during the entire study period. The protocol was approved by the Human Research Ethics Committee of the Faculty of Medicine, Ramathibodi Hospital, Mahidol University. All subjects gave written informed consent after the aims and procedures for the study were explained.

Study Design and Procedures

A single oral dose of either 300 or 500 mg of levofloxacin was administered in a controlled, randomized, 2 x 2-crossover design on two different occasions. The washout period was 1 week. All subjects were asked to fast overnight or not less than 8 hours before drug administration. On the study day, levofloxacin 300 or 500 mg was administered orally with 250 mL of water. Meals were served 4 hours post dose. Blood samples (5 mL) were withdrawn from a heparinized catheter fixed on the subject's arm, prior to and at 0.25, 0.5, 0.75, 1, 1.25, 1.5, 2.0, 2.5, 3, 4, 8, 10, 24 and 48 hours after dosing. All blood samples were kept in heparinized tubes and then centrifuged at 5,000 rpm for 5 minutes. The plasma was separated and kept at -80°C until analysis.

Quantitative Drug Analysis

Plasma levofloxacin concentrations were determined by high performance liquid chromatography (HPLC), modified from the method of Basci et al[5], using the HPLC model LC-10 AD (Shimadzu Co., Japan). A reversed-phase column, Shim-Pack CLC-ODS® C_{18}, 5 μm (4.6 mm x 25 cm) was used as an analytical column. A mixture of acetonitrile, methanol and 0.4 M citric acid in the ratio of 1:6:20 was used as the mobile phase. Pipemedic acid 60 μg/mL was applied as an internal standard. Peak detection was performed by a fluorescence detector at an excitation wavelength of 290 nm and an emission wavelength of 500 nm. Calibration plots were constructed by least-square linear regression of peak area ratio on levofloxacin concentration, weighted by the reciprocal of the variance[6]. These were linear ($r = 0.9998$) for levofloxacin concentrations between 0.02 and 5 μg/mL. Between-day and within-day imprecision were less than 12 per cent (CV) while inaccuracy was less than 14 per cent and recovery was up to 100 per cent. Plasma samples which contained concentrations above the detection range were reassayed by dilution.

Preparation of Samples

One hundred and fifty microlitres of plasma were mixed with 50 μL of pipemidic acid

solution, an internal standard, and 600 µL of methanol by vortex mixer for 30 seconds, then centrifuged at 5,000 rpm for 5 minutes. Twenty microlitres of the clear supernatant were injected into the HPLC system to quantitate levofloxacin concentration.

Pharmacokinetic Analysis

PCNONLIN (version 4, SCI Software, Lexington, KY, USA) was used to estimate the pharmacokinetic parameters based on a linear, 2-compartment model with first-order absorption with lag time and first-order elimination. Nonlinear regression analyses were performed using a weighting scheme of the dependent variable (plasma levofloxacin concentration, c) of 1/c to obtain the best fit. The equation used to describe the relationship between plasma levofloxacin concentration (c) and time (t) was

$$c(t) = Ae^{-\alpha(t-t_{lag})} + Be^{-\beta(t-t_{lag})} + Ce^{-k_a(t-t_{lag})}$$

where k_a = first-order absorption rate constant
α = distribution rate constant
β = first-order, elimination rate constant from the entire body
t_{lag} = lag time
A,B,C = constant values.

The estimated parameters were t_{lag}, k_a, absorption half-life ($t_{1/2ka}$), α, β, apparent volume of distribution of the central compartment (V/F), distribution half-life ($t_{1/2\alpha}$), elimination half-life ($t_{1/2\beta}$) and constant values for A and B.

Area under the plasma level *versus* time curve (AUC) from 0 to 48 hours (AUC_{0-48}), AUC from 0 hour to infinity ($AUC_{0-\infty}$), apparent total body clearance (CL/F), apparent volume of distribution at steady state (V_{ss}/F) and mean residence time (MRT) were calculated by the MK model program (version 4.84 Biosoft, Cambridge, UK), based on noncompartmental moment analysis method. The AUC values were calculated based on the summation of linear and log trapezoidal method[7]. The CL/F values were determined from dose/$AUC_{0-\infty}$. The V_{ss}/F values were calculated from CL/F multiplied by MRT which was determined from $AUMC_{0-\infty}/AUC_{0-\infty}$ where $AUMC_{0-\infty}$ is the area under the first moment of the plasma concentration versus time curve from 0 hour to infinity[8]. Maximum plasma concentration (C_{max}) and time to reach the maximum plasma concentration (T_{max}) were obtained from the raw data of the plasma concentration-time profile.

RESULTS

Twelve healthy male volunteers participated in the study. Their age, weight and height (mean ± SD) were 22.92 ± 2.50 years (range 20-28

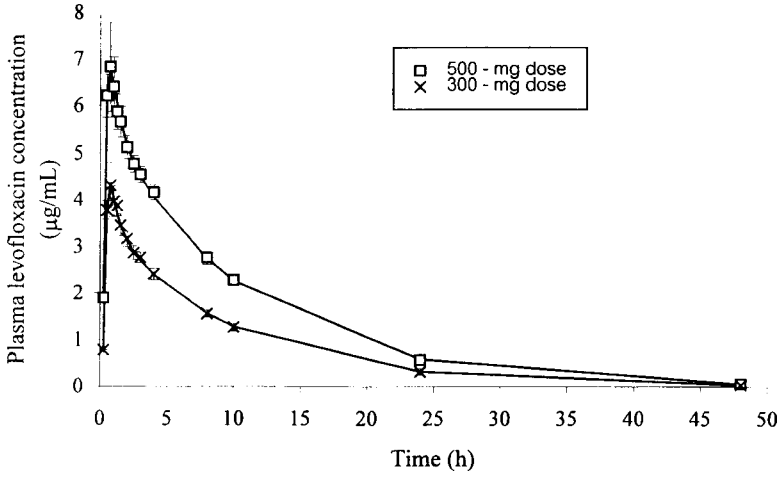

Fig. 1. Mean ± SEM plasma concentration-time profile with the line of best fit of levofloxacin after a single oral dose administered to 12 healthy Thai male volunteers. The line of best fit was generated from model fitting by PCNONLIN (version 4, SCI software, Lexington, KY, USA).

years), 57.92 ± 10.00 kg (range 49-85 kg) and 169.33 ± 4.87 cm (range 160-175 cm), respectively. No adverse effects were reported by any subject and all completed the study.

Almost all the plasma concentration-time profiles of levofloxacin from all subjects in the present study were well described by a linear, 2-compartment open model with first-order absorption with lag time and first-order elimination, except for one subject. His concentration-time profile after receiving a 500-mg dose was more appropriately described by a 1-compartment open model with first-order absorption with lag time and first-order elimination. The mean plasma concentration-time profiles of levofloxacin with the best fit from each dose are illustrated in Fig. 1. The pharmacokinetic parameters are summarized in Table 1. The absorption of levofloxacin was delayed with a short lag time of about 15 minutes. Once the absorption started, it was very rapid with a high rate constant, resulting in T_{max} of less than 0.8 hour for both doses (Table 1). C_{max} and AUC increased with dose. AUC_{0-48} was close to $AUC_{0-\infty}$ for both doses. Distribution rate constants were about 2 h^{-1} for both doses. This resulted in high apparent V_{ss}/F of approximately 1.5 L/kg. The elimination phase for both doses revealed an elimination rate constant of about 0.1 h^{-1} resulting in long $t_{1/2\beta}$ of 7-8 h. Apparent total body clearance (CL/F) was 8.64 ± 0.41 L/h and 8.31 ± 0.37 L/h for a 300-mg and a 500-mg dose, respectively, while the MRT of both doses was about 10.5 hours.

DISCUSSION

The pharmacokinetic profiles of levofloxacin in Thai subjects described by the 2 -compartment open model corresponded with the model proposed in previous pharmacokinetic studies of levofloxacin[9-11]. This is consistent with the distribution property of the drug, which revealed a high V_{ss}/F of approximately 1.5 L/kg for both doses. This was larger than those reported by other investigators which were between 1.1-1.3 L/kg (Table 2). The results support the finding that levofloxacin is well distributed in various body tissues and fluids with only 24-38 per cent of plasma protein binding [12] and suggest that the drug is distributed in a relatively larger area in our subjects than in Western people.

Levofloxacin was absorbed very rapidly after a short lag time of about 15 minutes. This lag time probably reflects the disintegration and dissolution of the tablet before systemic absorption. No other reports have mentioned such a characteristic of this drug, but other investigators did not start sampling until 30 minutes after dosing and assumed the absorption rate of the drug to be zero order and completed at T_{max}[9,13-15]. Our sampling time

Table 1. Pharmacokinetic parameters (mean ± SEM) of levofloxacin after a single oral administration to 12 healthy Thai male volunteers.

Pharmacokinetic parameter	Dose of levofloxacin (mg)	
	300	500
t_{lag} (h)	0.25 ± 0.03	0.26 ± 0.03
C_{max} (μg/mL)	4.83 ± 0.33	7.75 ± 0.71
T_{max} (h)	0.73 ± 0.08	0.77 ± 0.08
AUC_{0-48} (μg x h/mL)	35.26 ± 1.95	60.83 ± 2.74
$AUC_{0-\infty}$ (μg x h/mL)	35.77 ± 2.06	61.57 ± 2.84
k_a (h^{-1})	13.13 ± 3.50	12.22 ± 3.60
$t_{1/2ka}$ (h)	0.16 ± 0.07	0.17 ± 0.03
V/F (L)	48.07 ± 4.82	52.84 ± 6.21
V_{ss}/F (L/kg)	1.53 ± 0.06	1.49 ± 0.05
α (h^{-1})	1.83 ± 0.34	2.26 ± 0.28
$t_{1/2\alpha}$ (h)	1.18 ± 0.53	0.53 ± 0.23
ß (h^{-1})	0.09 ± 0.01	0.10 ± 0.00
$t_{1/2\beta}$ (h)	7.99 ± 0.57	7.14 ± 0.31
MRT (h)	10.43 ± 0.43	10.49 ± 0.38
CL/F (L/h)	8.64 ± 0.41	8.31 ± 0.37
A	115.21 ± 81.61	99.19 ± 80.67
B	2.80 ± 0.35	5.90 ± 0.23

Table 2. Pharmacokinetic parameters (mean ± SEM) of levofloxacin after a single oral administration of 300 and 500 mg in our study compared with those reported after a single oral dose of 350 mg in HIV patients[9,13] or a single oral dose of 500 mg in healthy Western volunteers[14-16].

Pharmacokinetic parameter	Dose of levofloxacin (mg)			
	300	350 [a]	500	500 [b]
C_{max} (μg/mL)	4.83 ± 0.33 [c]	4.79 ± 0.45 [9] c 3.82 ± 0.32 [13] c	7.75 ± 0.71 [c]	5.52 ± 0.29 [14] c 5.19 ± 0.38 [15] c 5.9 ± 0.27 [16] c
T_{max} (h)	0.73 ± 0.08 [c]	1.00 ± 0.27 [9] c 1.1 ± 0.20 [13] c	0.77 ± 0.08 [c]	1.5 ± 0.17 [14] c 1.3 ± 0.16 [15] c 1.0 [16] c
$AUC_{0-\infty}$ (μg x h/mL)	35.77 ± 2.06	29.94 ± 3.00 [9] 30.1 ± 0.73 [13]	61.57 ± 2.84	47.5 ± 2.83 [14] 47.7 ± 2.40 [15] 50.5 ± 1.65 [16]
V_{SS}/F (L/kg)	1.53 ± 0.06	1.31 ± 0.09 [9] d 1.28 ± 0.12 [13] d	1.49 ± 0.05	1.13 ± 0.05 [14] d 1.28 ± 0.05 [15] d
$t_{1/2\beta}$ (h)	7.99 ± 0.57	5.66 ± 0.31 [9] e 6.2 ± 0.37 [13]	7.14 ± 0.31	6.0 ± 0.26 [14] 7.4 ± 0.28 [15] 6.2 ± 0.33 [16]
MRT (h)	10.43 ± 0.43	8.17 ± 0.46 [9] f	10.49 ± 0.38	NA
CL/F (L/h)	8.64 ± 0.41	12.3 ± 1.24 [9] 11.4 ± 0.29 [13]	8.31 ± 0.37	10.92 ± 0.61 [14] 10.5 ± 0.55 [15] 10.1 ± 0.33 [16]

a : Studies of Goodwin et al [9] and Chien et al [13].
b : Studies of Chien et al [14], Chien et al [15] and Lee et al [16].
c : From visual inspection of the plasma drug concentration versus time data.
d : Determined from (dose/$AUC_{0-\infty}$) x MRT.
e : Determined as effective $t_{1/2}$ = 0.693 x MRT.
f : Determined as ($AUMC_{0-\infty}/AUC_{0-\infty}$)-($T_{max}/2$).
NA : Not available.

was started earlier at 15 minutes after dosing which revealed the time lag. T_{max} of about 0.8 hour for both doses in our study was relatively faster than those reported by others, which were between 1 and 1.5 hours[9,13-16] (Table 2). This also confirmed the rapid absorption of the drug. The increase in C_{max} and AUC with dose agreed with the linear pharmacokinetics of this drug described for doses of 50-1000 mg administered as a single oral dose in healthy Western volunteers[17]. AUC_{0-48} was almost equal to $AUC_{0-\infty}$ for both doses, indicating that our sampling time of up to 48 hours covered almost all the drug absorbed in the body.

In comparison to other studies (Table 2), our mean C_{max} (4.83 μg/mL) after a single oral dose of 300 mg was comparable to or higher than those obtained from a single, 350 mg dose orally administered to HIV patients[9,13]. On the other hand, a reported C_{max} of only 2.8 μg/mL after a 250-mg dose administered to healthy Western volunteers[4] was much lower than our C_{max} after a 300-mg dose compared in a dose-proportional manner. Moreover, after a single 500 mg dose orally administered in healthy Western volunteers, the mean C_{max} was between 5.2 and 5.9 μg/mL (Table 2), whereas, in our study it was much higher (7.75 μg/mL). Similar characteristics were also seen from the extent of absorption (AUC). However, when dose per kg bodyweight of the subjects in all those studies were considered, it was found that our Thai male subjects received a higher dose than Western subjects (approximately 5.2 mg/kg and 8.64 mg/kg after a 300-mg and a 500-mg dose in our subjects; 4.6 mg/kg after a 350-mg and 7 mg/kg after a 500-mg dose in Western subjects). Therefore, the higher C_{max} and $AUC_{0-\infty}$ in our subjects may be the result of the higher dose per kg bodyweight used.

The elimination characteristics of levofloxacin showed that the mean CL/F obtained in this study was less than previously reported values (Table 2). This indicates that levofloxacin was

eliminated from our subjects more slowly than from Western people. Our clearance tends to be close to that of Japanese subjects who had CL/F of 9.6 L/h after a 100-mg dose[12]. The effect of race thus may be suspected for such differences and may indicate a different dosage regimen. This lower clearance was also reflected in the longer $t_{1/2\beta}$ of 7-8 hours in our study compared to that previously reported of 6-7.4 hours. It could be postulated that in addition to the higher dose per kg bodyweight, the rapid absorption and the lower clearance of the drug should contribute to the higher C_{max} in our subjects. Some may argue that our larger V_{ss}/F should not allow for such a high C_{max}, however, if the magnitude of difference of clearance of the drug between our subjects and Western people is considered, it seems that this factor is relatively larger than that of V_{ss}/F. Thus, the clearance should contribute more significantly to the level of the drug while the larger V_{ss}/F should contribute to the longer time the drug spends in the body. This was confirmed by the longer MRT, the average time for all the drug molecules to reside in the body, demonstrated in our study. This noncompartmental pharmacokinetic parameter has been reported as postabsorption MRT, calculated as $(AUMC_{0-\infty}/AUC_{0-\infty})-(T_{max}/2)$[9,13-15] and the mean value reported by Goodwin et al[9] was 8.17 hours. This was shorter than our reported MRT, which covered both absorption and disposition phases as it was calculated as $AUMC_{0-\infty}/AUC_{0-\infty}$. When the postabsorption MRT was determined using our data, it was 10.1 hours. This was still longer than the previously reported postabsorption MRT; this thus supports our conclusion. The postabsorption MRT was also used to determine V_{ss}/F in other studies [9,13-15] and may therefore have contributed to the lower V_{ss}/F of the others. Again, when this MRT was recalculated, the reported V_{ss}/F was still relatively lower than in our study. So the previous explanation is still likely. The MRT value indicates how long the drug molecules stay in the peripheral compartment and clinically this may suggest the dosing interval of the drug[18]. For levofloxacin, both the relatively long $t_{1/2\beta}$ and MRT contribute to the once daily dosage regimen.

As we know that fluoroquinolone antibiotics have a concentration-dependent effect[19, 20], a high C_{max} should be beneficial for clinical and microbiological outcomes in levofloxacin therapy. Accordingly, the higher C_{max} obtained in our study should have significant implications in terms of dose recommended, which may be different for Asian and Western people. It has been proposed that the killing activity of levofloxacin correlates best with the ratio of C_{max} to the MIC and that this ratio should be more than 12.2[11]. This however, depends on the MIC_{90} of the drug for pathogenic microorganisms in a particular region. Levofloxacin and other newer fluoroquinolones are now recommended as first-line therapy for CAP and other respiratory tract infections caused by *Streptococcus pneumoniae, Haemophilus influenzae, Chlamydia pneumoniae, Mycoplasma pneumoniae* or *Legionella pneumophila*[4]. The median MIC_{90} of levofloxacin reported in the literature[4] for these pathogens were: 0.032 μg/mL (range ≤0.008->2 μg/mL) for *H. influenzae*, 0.05 μg/mL (range 0.125-0.5 μg/mL) for *C. pneumoniae*, 0.5 μg/mL (range 0.025-0.5 μg/mL) for *M. pneumoniae* and 0.03-0.125 μg/mL (range 0.003-1 μg/mL) for *L. pneumophila*. Thus, our C_{max} of 4.83 μg/mL after a 300 mg single dose should cover those common pathogens in respiratory tract infections, according to the C_{max}:MIC ratio mentioned previously. For penicillin-resistant *S. pneumoniae*, the MIC_{90} of levofloxacin recently reported in Thailand was 2 μg/mL[21]. This indicates that a higher C_{max} is required for a successful therapy, i.e. that obtained from our single 500 mg dose (C_{max} : 7.75 μg/mL). For other indications, e.g. complicated UTIs, *Escherichia coli*, the common pathogen is also susceptible to levofloxacin with a median MIC_{90} of 0.12 μg/mL (range ≤0.008-256 μg/mL)[4], while in SSTIs, *Staphylococcus aureus* (methicillin-sensitive) is susceptible to levofloxacin with a median MIC_{90} of 0.5 μg/mL (range 0.03-12.5 μg/mL)[4]. This achievement of a suitable maximum concentration after a single dose as well as a relatively long $t_{1/2\beta}$ and MRT support the once daily dosage of levofloxacin. Moreover, it has been demonstrated that levofloxacin administered as a single daily dose, rather than in divided doses, provides more rapid bactericidal activity[17].

The mean plasma concentration at 24 hours after a 300-mg dose of levofloxacin (0.321± 0.035 μg/mL) was greater than the MIC_{90} for most Gram-negative bacteria but did not cover the MIC_{90} for Gram-positive bacteria and anaerobic bacteria (median MIC_{90} 1-16 μg/mL)[4]. The mean plasma concentration at 24 hours after a 500-mg dose (0.574±0.055 μg/mL) covered the MIC_{90} for

most Gram-negative bacteria and some Gram-positive bacteria but could not cover anaerobic bacteria. Nonetheless, levofloxacin has been reported to have a postantibiotic effect, at least on methicillin-sensitive *S. aureus*, methicillin-resistant *S. aureus*, *S. epidermedis*, *S. pneumoniae* and *E. coli* (4,12). This phenomenon may have clinical importance, particularly after drug concentration falls below the MIC. Furthermore, properties affecting tissue penetration, particularly in areas of infection, e.g. lung, maxillary sinus, epithelial lining or skin (14), and the uptake of the drug into phagocytic cells may contribute to its effect, even after the blood concentration has already decreased. This intracellular accumulation may enhance not only drug activity against intracellular pathogens, but also its activity against extracellular pathogens, as it can act as a reservoir to maintain high, sustained concentrations of the drug within tissues and fluids at the site of infection(17).

Thus, levofloxacin as a single daily dose of 300 mg shows pharmacokinetic properties that seem to be appropriate for those respiratory tract infections caused by most Gram-negative and atypical bacteria or for complicated UTIs caused by Gram-negative bacteria or for SSTIs caused by Gram-positive bacteria. In complicated UTIs or pyelonephritis or some conditions of AECB, a lower dose of 250 mg daily has already been recommended in the US and Europe(4). In cases of UTIs this may be possible since a high urine level of levofloxacin has usually been obtained(4). In severe cases or *S. pneumoniae* infection, however, a higher dose of 500 mg as a single daily dose should be recommended. Unfortunately, levofloxacin has no or only limited activities against some Gram-negative bacteria, e.g. *Pseudomonas aeruginosa, Serratia* spp. and most anaerobic bacteria. Therefore, it has no role in infections such as nosocomial infection.

In conclusion, the present study demonstrated that pharmacokinetics of levofloxacin in Thai people are different from those of Western people. Higher C_{max} and relatively lower clearance were obtained in our subjects. The results revealed from our first pharmacokinetic study of a single dose of levofloxacin in healthy Thai subjects are a promising guide for the treatment of Thai patients. However, the effectiveness of a regimen composed of 300 mg once daily for 7-14 days, as recommended in Thailand, in those infections caused by our common pathogens as well as long term safety profiles of the drug should be further confirmed.

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เภสัชจลนศาสตร์ของยา levofloxacin ในอาสาสมัครไทยเพศชายสุขภาพดี

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ทำการศึกษาเภสัชจลนศาสตร์ของยา levofloxacin ซึ่งเป็น fluoroquinolone ตัวใหม่ในอาสาสมัครไทยเพศชายสุขภาพดี จำนวน 12 คน อายุเฉลี่ย (SD) 22.92 (2.50) ปี โดยสุ่มแบ่งกลุ่มอาสาสมัครเป็น 2 กลุ่ม ให้รับประทานยาขนาด 300 มิลลิกรัม หรือ 500 มิลลิกรัม ครั้งเดียว ข้ามสลับกันโดยมีระยะห่างของการรับประทานยา 1 สัปดาห์ อาสาสมัครต้องอดอาหารมาก่อนรับประทานยาเป็นเวลาอย่างน้อย 8 ชั่วโมง ทำการเจาะเลือดก่อนรับประทานยา และตั้งแต่เวลา 0.25 ถึง 48 ชั่วโมงหลังรับประทานยา วิเคราะห์ความเข้มข้นของยา levofloxacin ในพลาสมาด้วยวิธี HPLC

เภสัชจลนศาสตร์ของยา levofloxacin อธิบายได้ดีด้วย linear, 2–compartment open model ที่มีการดูดซึมและกำจัดยาแบบ first–order และมี lag time ก่อนการดูดซึม ค่าเฉลี่ย ± SEM ของระดับยาสูงสุดในพลาสมา ภายหลังรับประทานยาขนาด 300 มิลลิกรัม และ 500 มิลลิกรัม มีค่า 4.83 ± 0.33 และ 7.75 ± 0.71 ไมโครกรัม/มิลลิลิตร ตามลำดับ โดยเวลาที่ระดับยาขึ้นสูงสุดในพลาสมามีค่า 0.7 ถึง 0.8 ชั่วโมงสำหรับยาทั้ง 2 ขนาด ค่าเฉลี่ย ± SEM ของพื้นที่ใต้เส้นกราฟระหว่างระดับยาในพลาสมากับเวลา มีค่า 35.77 ± 2.06 ไมโครกรัม x ชั่วโมง/มิลลิลิตร สำหรับขนาด 300 มิลลิกรัม และ 61.57 ± 2.84 ไมโครกรัม x ชั่วโมง/มิลลิลิตร สำหรับขนาด 500 มิลลิกรัม ยากระจายตัวได้ดีโดยมีค่าการกระจายตัวที่ steady state ประมาณ 1.5 ลิตร/กิโลกรัมน้ำหนักตัว อัตราการกำจัดยามีค่าเฉลี่ย ± SEM เท่ากับ 8.64 ± 0.41 ลิตร/ชั่วโมง สำหรับขนาด 300 มิลลิลิตร และ 8.31 ± 0.37 ลิตร/ชั่วโมง สำหรับขนาด 500 มิลลิกรัม ค่าครึ่งชีวิตของยามีค่ายาว 7 ถึง 8 ชั่วโมง โดยค่าเฉลี่ย ± SEM ของการที่ยาจะอยู่ในร่างกายมีค่า 10.43 ± 0.43 ชั่วโมง และ 10.49 ± 0.38 ชั่วโมง สำหรับขนาด 300 มิลลิกรัม และ 500 มิลลิกรัม ตามลำดับ ผลการศึกษาแสดงว่ายาขนาด 300 มิลลิกรัม รับประทานวันละ 1 ครั้ง สามารถให้ระดับยาสูงสุดในพลาสมาที่ครอบคลุมเชื้อแบคทีเรียแกรมลบ และ atypical bacteria (median MIC_{90} 0.032–0.5 ไมโครกรัม/มิลลิลิตร) ที่พบบ่อยในการติดเชื้อขั้นอ่อนถึงปานกลางในระบบทางเดินหายใจ หรือการติดเชื้อแบบซับซ้อนในระบบทางเดินปัสสาวะ และแบคทีเรียแกรมบวก (median MIC_{90} 0.5 ไมโครกรัม/มิลลิลิตร) ที่พบบ่อยในการติดเชื้อทางผิวหนังและเนื้อเยื่ออ่อน สำหรับการติดเชื้อขั้นรุนแรง หรือติดเชื้อ *Streptococcus pneumoniae* (MIC_{90} 2 ไมโครกรัม/มิลลิลิตร) ควรใช้ยาขนาด 500 มิลลิกรัม

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