An Open, Non Comparative Study of Ofloxacin I.V. on the Treatment of Acute Symptomatic Urinary Tract Infection

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Abstract

The clinical efficacy and the safety of ofloxacin I.V. in 35 acute symptomatic urinary tract patients were evaluated. The drug was intravenously administered, 400 mg starting dose then 200 mg once-daily for 3-5 days. The therapeutic success rate and eradication rate in UTI case were 100 per cent in all cases when evaluated immediately after completion of drug treatment, therapeutic success rate and eradication rate at the follow-up evaluation were 97.2 per cent and 91.6 per cent respectively. Also, 5 cases of acute bronchitis and 2 salmonellosis were also administered intravenously, 400 mg once-daily dose and 400 mg twice daily dose respectively. No serious side effects of ofloxacin I.V. therapy were observed in any of our patients.

Key word : Ofloxacin, UTI, Bronchitis, Salmonellosis

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Ofloxacin is a broad spectrum fluoroquinolone agent which acts by inhibiting bacterial DNA gyrase, with an excellent penetration into various tissues, has very good tolerability and an extended serum elimination half-life[1-5]. Ofloxacin, one of the most commonly prescribed fluoroquinolone antibacterials, is active in a range of infections, and a very effective drug for the treatment of acute infection caused mainly by gram-negative organisms such as enterobacteriaceae, *Haemophilus* and *Neisseria* spp[6-10]. Ofloxacin is usually administered twice daily either orally or intravenously. Recently a few trials in which ofloxacin was administered once daily have been reported[11-15]. In our study, patients who were suffering from acute symptomatic UTI, received 400 mg ofloxacin I.V. start-

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ing dose on the first day and 200 mg as a once daily-dose on the following day. Intravenous administration attains a reliable level in urine that achieves therapeutic efficacy(2) and decreases the problem of G.I. absorption. The aims of this study were to evaluate the clinical and bacteriological efficacy of once-daily ofloxacin I.V. in patients with acute symptomatic urinary tract infection.

MATERIAL AND METHOD

Patients who visited the Department of Family Medicine and Department of Medicine, Ramathibodi Hospital were eligible for inclusion to the study if they gave an informed consent to participate in the study. Our subjects were 42 patients with acute uncomplicated cystitis who presented with symptoms suggestive of an acute lower urinary tract infection (such as dysuria, frequency, urgency and occasional hematuria) and who also had pyuria (WBC count ≥ 10 cells/ high power field in mid stream urine, which was ultimately confirmed bacteriologically (≥ 10^5 cfu/ml organisms). In addition, 5 cases with acute exacerbation of chronic bronchitis and 2 cases with other infections (Enteric fever and Salmonella arthritis) were also studied. A diagnosis of bronchitis was considered in patients with a purulent sputum sample, that, on gram stain showed bacteria consistent with WBC count (CBC) ≥ 10,000 cells/μl. Exclusion criteria included pregnancy and lactating women, hypersensitivity to quinolones, having received antibiotics within the previous 7 days, or had impaired renal and liver function. Physical examination, CRP, ESR, blood chemistry, hematology investigation were performed before initial therapy and on the last treatment day. Urinalysis and urine culture were done at each visit. Follow-up examinations were performed 7-14 days after completion of drug treatment. Standard laboratory procedures were used for the isolation and identification of pathogens. Minimal inhibitory concentration (MICs) for the infecting pathogens were determined by tube dilution method and the E-Test was used for determining MICs of bronchitis pathogens.

Ofloxacin, (Tarivid® I.V. produced by Daiichi Pharmaceutical Co., Ltd) 400 mg starting dose and then a 200 mg once-daily dose was administered intravenously over 45 minutes for 3-5 days in UTI patients, 400 mg ofloxacin as a once-daily dose for 5 days in bronchitis and 400 mg as a twice-daily dose for 14 days in Enteric fever and 28 days in Salmonella arthritis.

RESULTS

Of the 42 acute symptomatic urinary tract infection patients enrolled, 7 UTI cases were excluded from efficacy evaluation because of renal stone(4), lost to follow-up(1), the causative pathogen was resistant to ofloxacin before the initial treatment(2). A total of 42 patients were 5 males and 37 females with mean age 37.2 (range 16-71 years). *E. coli* was the most common etiology of UTI (58.3%) and followed by *Staphylococcus saprophyticus* (13.9%), *Klebsiella pneumoniae* (8.3%), Coagulase negative *Staphylococci* (8.3%) and the other organisms 11.2 per cent. Pyuria and bacteriuria (as proved by culture) were not presented at the second treatment day in most of the patients. All patients were clinically cured or improved by 1 to 2 days after initiation of therapy. Overall clinical efficacy was evaluated immediately after completion of drug treatment (Table 1). The overall efficacy rate and the total eradication rate were 100 per cent (85.7 excellent and 14.3 good response), pyuria decreased in 4 patients and unchanged in 1 case but their urine culture showed no growth since the second day of therapy throughout the time of follow-up, except for 1 case with *E.coli* which was eradicated after completion of drug treatment and relapsed on the follow-up examination.

Table 2 shows the follow-up results of UTI (7-14 day after therapy), it shows that intravenous ofloxacin 400 mg starting dose and then 200 mg once daily achieved 97.2 per cent efficacy in all cases. Of the 35 patients, the response was judged to be excellent in 24 (68.6%), good in the other 10 (28.6%) and poor in 1 (2.8%). Bacteriological eradication rates were also good (91.6%), with complete eradication of 19/21 strains of *E.coli*, 5/5 of *Stap. saprophyticus*, 2/3 of *Kleb. pneumoniae*, 3/3 coag. negative *Stap.* and 1/1 of each *Stap. aureus*, *Proteus mirabilis*, *Strep. enterococci* and *Enterobacter* spp. Three cases in which *E.coli* and *Kleb. pneumoniae* were the causative pathogens (were eliminated since the second day of therapy), two developed asymptomatic bacteriuria (replaced with *Strep.* group B and *Strep.* not gr. A,B,D) without pyuria and one developed pyuria and relapsed with 10^5 *E.coli*, however, this strain was sensitive to ofloxacin.

In this study, ofloxacin 400 mg as a once-daily and twice-daily dose was also administered intravenously in bronchitis patients(5) and salmo-

Table 1. Overall clinical efficacy for UTI (last day of therapy).

	Pyuria			Total Bacteriuria	
	Cleared	Decreased	Unchanged	No	%
Bacteria					
Eliminated	30[A]	4[G]	1[G]	35	100
Decreased	-	-	-		
Replaced	-	-	-		
Unchanged	-	-	-		
Total pyuria	30	4	1		
Overall efficacy rate	(85.7%)	(11.4%)	(2.9%)	35/35	100

A = Excellent (n = 30), G = Good (n = 5), P = Poor (n = 0)

Table 2. Clinical and Bacteriological effectiveness of ofloxacin I.V. (follow-up results).

Infections	No. of Case	Infection Agent	n	Clinical Cure(n)	Bacteriological eradication(n)	MIC_{90}
Urinary tract infection	35	*E. coli*	21*	19	19#	0.1
		Stap.saprophyticus	5	5	5	1
		Stap. coag.negative	3	3	3	0.5
		Kleb.pneumoniae	3	3	2#	0.25
		Stap.aureus	1	1	1	1
		Strep.enterococci	1	1	1	1.5
		Proteus mirabilis	1	1	1	0.06
		Enterobacter spp.	1	1	1	0.064
Bronchitis	5	*H. influenzae*	1	1	1	0.047
		Kleb. pneumoniae	1	1	1	0.19
		Proteus mirabilis	1	1	1	0.125
		B. catarrhalis	2	2	2	ND
Enteric Fever	1	*Salmonella paratyphi* A	1	1	1	ND
Salmonella arthritis	1	*Salmonella* group D	1	1	1	0.06

*one case had 2 causative agents. # replaced with *Strep.* Group B, *Strep.* not group A,B,D and relapsed with *E.coli*

nellosis patients(2) respectively. All patients were clinically cured and the pathogen isolates were completely eradicated. In addition, one patient who complained of fever, chills, cough, a large amount of sputum and whose chest X-ray revealed RLL and LUL infiltrated with cavity but had a three day sputum examination which showed no acid fast. Only one day after starting 400 mg I.V. daily dose, the productive cough was decreased, temperature dropped from 37.8°C to 36.8°C and the chest X-ray showed the cavity decreasing in size after a few days. Twelve days after initial therapy she was diagnosed as pulmonary tuberculosis by the PCR technique and AFB staining (rare AFB positive). AFB and culture turned negative at 1 and a half months after combination therapy with ofloxacin and TB drug.

Most patients tolerated ofloxacin well, no biochemical abnormalities and no serious adverse reactions were found in this study. Only two patients complained of dizziness and headache, which occurred only on the first day of therapy.

DISCUSSION

Verho[2] demonstrated the clinical pharmacology of ofloxacin, that ofloxacin is rapidly and almost completely penetrated and absorbed into tissue and body secretions. The urinary concentrations are dose-dependent, but the proportion of the dose excreted *via* the kidneys remains approximately constant, 80 per cent or more of the dose being recovered as unchanged ofloxacin. The concentration of ofloxacin after a single 100 mg dose is higher at any time in the following 24 hours than

the MIC values for most common microorganisms responsible for urinary infection.

Ostri[13] compared the clinical and bacteriological effect of ofloxacin 200 mg once daily *versus* 100 mg twice daily in patients with complicated urinary tract infections. The result was that 200 mg once daily was at least as effective as treatment with 100 mg twice daily.

The data obtained in our study indicated that once daily intravenous ofloxacin 400 mg starting dose then 200 mg once daily dose for UTI are effective and safe. The symptoms were cured or improved by 1 to 2 days after initial therapy. The rapid relief of clinical symptoms and the dose of ofloxacin used in this study, did not provoke significant side effects. We concluded that ofloxacin I.V. 400 mg starting dose then 200 mg as a once daily dose, was well tolerated and effective in the treatment of UTI. In the treatment of bronchitis and Salmonellosis we used 400 mg once-daily and twice-daily doses respectively, and the outcomes were successful. However, the efficacy and safety of intravenous ofloxacin in the treatment of bronchitis and salmonellosis remain to be determined.

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การศึกษาประสิทธิภาพของยาโอฟล็อคซาซิน ชนิดฉีด ในการรักษาผู้ป่วยติดเชื้อระบบทางเดินปัสสาวะ

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การศึกษาประสิทธิภาพและความปลอดภัยในการได้รับยาโอฟล็อคซาซินชนิดฉีด วันละครั้งเดียว ในผู้ป่วยที่ได้รับการวินิจฉัยว่า เป็นโรคติดเชื้อในระบบทางเดินปัสสาวะ 35 ราย ผู้ป่วยติดเชื้อในระบบทางเดินปัสสาวะจะได้รับยาโอฟล็อคซาซินชนิดฉีดวันแรก 400 มิลลิกรัม และ 200 มิลลิกรัมต่อวันในวันต่อไป 3–5 วัน ผลการรักษาพบว่าอัตราการตอบสนองต่อการรักษาโดยยาโอฟล็อคซาซินชนิดฉีด และอัตราการกำจัดเชื้อของผู้ป่วยติดเชื้อในระบบทางเดินปัสสาวะเท่ากับร้อยละ 100 เมื่อทำการประเมินทันทีที่ได้รับยาครบ และเมื่อประเมินในการติดตามการรักษา พบว่าผู้ป่วยตอบสนองต่อการรักษา 97.2% และอัตราการกำจัดเชื้อ เท่ากับ 91.6% นอกจากนี้ยังมีผู้ป่วยระบบทางเดินหายใจ 5 ราย และผู้ป่วยติดเชื้อ *Salmonella* 2 ราย ได้รับยาโอฟล็อคซาซินชนิดฉีด 400 มิลลิกรัม วันละครั้ง และ 400 มิลลิกรัม วันละ 2 ครั้ง ตามลำดับ ไม่พบผลข้างเคียงใด ๆ ในผู้ป่วยที่ได้รับยาโอฟล็อคซาซินชนิดฉีด ในการศึกษาครั้งนี้

คำสำคัญ : โอฟล็อคซาซิน, ภาวะติดเชื้อระบบทางเดินปัสสาวะ, หลอดลมอักเสบ, ซัลโมเน็ลโลสิส

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