

尿路・性器感染症に対する pazufloxacin の臨床的検討

菅 政治・上間建造[#]・香川 征

徳島大学医学部泌尿器科学教室*

(主任: 香川 征教授)

(*現 小松島赤十字病院泌尿器科)

湯浅 誠

高松赤十字病院泌尿器科

(部長: 湯浅 誠)

複雑性尿路感染症22例, 単純性尿路感染症13例, 急性前立腺炎1例, 急性精巣上体炎1例に
対し, pazufloxacin (PZFX) を1回100~200mgを1日3回食後, 3~7日間経口投与し, 次の成績
を得た。

1) UTI薬効評価基準判定による慢性複雑性尿路感染症の総合臨床効果は, 著効14例, 有
効4例, 無効2例, 総合有効率90.0%であった。

2) 細菌学的効果は, 慢性複雑性尿路感染症では28株中26株(92.9%)が消失し, 急性単純
性尿路感染症の23株はすべてが消失した。

3) 自他覚的副作用は嘔気が1例認められた。臨床検査値の異常変動は, GPT・LAP, BUN
の軽度の上昇が各々1例認められた。

以上より, 本剤は尿路感染症に有効な薬剤と考えられた。

Key words: PZFX, 尿路感染症

新しく開発された経口用ピリドンカルボン酸系抗菌物質である pazufloxacin (PZFX) は, グラム陽性菌および *Pseudomonas aeruginosa* を含むグラム陰性菌に対して, 広範囲な抗菌スペクトラムを有し, ほとんどの菌種において既存の経口抗菌剤と比較し優れた抗菌力を示す¹⁾。今回, 尿路感染症に本剤を投与して, 臨床効果および副作用を検討したので報告する。

対象患者は1992年11月から1993年6月までに徳島大学医学部附属病院泌尿器科および高松赤十字病院泌尿器科で治療を受けた患者で, 治験の同意の得られた37例(19~81歳, 平均54.6歳)とした。症例の内訳は, 慢性複雑性尿路感染症22例, 急性単純性尿路感染症13例, 急性前立腺炎1例, 急性精巣上体炎1例であった。本剤の投与方法は, 1回100~200mgを1日3回食後, 3~7日間, 経口投与とした。本剤の薬効に影響を与える他の薬剤や処置の併用は行わなかった。総合臨床効果はUTI薬効評価基準(第3版)に従い判定した。また自他覚的症状, 膿尿, 細菌尿の推移から著効, 有効, やや有効, 無効の4段階評価による主治医独自の判定も併せて行った。安全性については, 本剤投与中および投与後の自他覚的副作用と, 投与前後の臨床検査値(末梢血, 肝機能, 腎機能, 血清電解質)異常変動により検討を行った。

慢性複雑性尿路感染症に対して, 本剤4~7日間投与

後の臨床成績をTable 1に示した。主治医判定では, 著効15例, 有効5例, 無効1例, 判定不能1例(投与終了直後受診せず)であった。UTI薬効評価基準判定から除外されたのは1例(真菌感染)であった。UTI薬効評価基準による総合臨床効果は著効14例, 有効4例, 無効2例, 総合有効率90.0%であった(Table 2)。UTI疾患病態別では単独菌感染の13例では著効11例, 有効2例で, 複数菌感染の7例では著効3例, 有効2例, 無効2例であった(Table 3)。細菌学的効果では, グラム陽性菌は8株中7株が消失し, グラム陰性菌は20株中19株が消失し, 全体で92.9%(26株/28株)の菌消失率であった。存続菌(MIC)は, *Streptococcus agalactiae* 1株(3.13 µg/ml), *Pseudomonas aeruginosa* 1株(>100 µg/ml)であった(Table 4)。投与後出現菌は, 20例中3例に3菌種4株が認められた(Table 5)。

急性単純性尿路感染症に対して本剤3~7日間投薬後の治療成績をTable 6に示した。全例で症状が消失し, 膿尿も正常化11例, 改善2例であった。本剤投与前に検出された11菌種23株は全株が消失した。主治医判定は著効11例, 有効2例であった。急性前立腺炎の1例, 急性精巣上体炎の1例は主治医判定は有効, 有効であった(Table 7)。本剤投与中および投与後の自他覚的副作用は嘔気が1例認められた。本剤投与後の臨床検査値の異

Table 1-1. Clinical summary of complicated UTI patients treated with pazufloxacin

Patient no.	Age (yr)	Sex	Diagnosis	Catheter (route)	UTI group	Treatment		Symptoms*	Pyuria*	Bacteriuria*			Evaluation**		Side effects	Remarks
			Underlying condition			dose (mg × /day)	duration (days)			species	count	MIC	UTI	Dr.		
1	62	F	CCP renal stone	—	G-3	100 × 3	7	++ —	≡ —	<i>P. mirabilis</i> —	10 ⁶ 0	≤0.025	excellent	excellent	—	
2	54	F	CCP ureteral stone	—	G-3	200 × 3	7	++ —	++ —	<i>E. cloacae</i> —	10 ⁴ 0	≤0.025	excellent	excellent	—	
3	64	F	CCP renal stone	—	G-3	200 × 3	7	— —	≡ —	<i>E. coli</i> —	10 ⁷ 0	0.05	excellent	excellent	—	
4	22	F	CCP ureteral stone	—	G-3	200 × 3	7	≡ —	≡ —	<i>E. aerogenes</i> —	10 ⁵ 0	0.05	excellent	excellent	—	
5	64	F	CCP renal stone hyperuricemia	—	G-3	200 × 3	4	— —	≡ —	<i>K. pneumoniae</i> <i>P. aeruginosa</i>	10 ⁷ <10 ³	≤0.025 >100	excellent	excellent	nausea	
6	67	M	CCC BPH urethral stricture	—	G-4	200 × 3	7	≡ +	≡ —	<i>E. coli</i> —	10 ⁶ 0	0.05	excellent	excellent	—	
7	75	M	CCC prostatic cancer	—	G-4	200 × 3	7	++ —	++ +	<i>E. faecalis</i> —	10 ⁶ 0	not done	moderate	good	—	
8	69	M	CCC prostatic cancer	—	G-4	100 × 3	7	— —	≡ —	<i>E. faecalis</i> —	10 ⁶ 0	3.13	excellent	excellent	—	
9	72	M	CCC neurogenic bladder	—	/	100 × 3	7	— —	≡ ±	<i>S. aureus</i> <i>S. aureus</i>	10 ⁶ 10 ⁴	0.2 0.2	/	unknown	—	
10	77	M	CCC neurogenic bladder	—		200 × 3	7	++ +	++ —	<i>C. freundii</i> —	10 ⁷ 0	0.39	excellent	excellent	—	
11	74	F	CCC neurogenic bladder	—	G-4	200 × 3	4	++ —	++ —	<i>E. coli</i> —	10 ⁶ 0	0.10	excellent	excellent	—	
12	70	M	CCC BPH	—	G-4	200 × 3	7	++ —	≡ —	<i>E. coli</i> —	10 ⁶ 0	≤0.025	excellent	excellent	—	
13	52	F	CCC neurogenic bladder	—	G-4	100 × 3	7	+ —	++ ±	<i>E. coli</i> —	10 ⁶ 0	≤0.025	moderate	good	—	
14	74	F	CCC neurogenic bladder	—	G-4	200 × 3	7	+ —	≡ —	<i>C. freundii</i> —	10 ⁷ 0	0.05	excellent	excellent	—	
15	43	F	CCP renal stone	—	G-6	200 × 3	7	≡ —	++ ±	<i>E. coli</i> <i>S. agalactiae</i> <i>S. epidermidis</i> <i>S. agalactiae</i>	10 ⁶ 10 ⁴	≤0.025 3.13 0.39 6.25	poor	good	—	
16	69	M	CCP urinary stone vesicoureteral reflux	—	G-6	100 × 3	7	+ —	++ ±	<i>E. coli</i> <i>E. faecalis</i> —	10 ⁷ 0	0.05 6.25	moderate	good	—	
17	65	F	CCC neurogenic bladder	—	G-6	100 × 3	7	+ —	++ —	<i>K. pneumoniae</i> <i>Klebsiella</i> sp. —	10 ⁴ 0	6.25 12.5	excellent	excellent	—	
18	68	F	CCC neurogenic bladder	—	G-6	100 × 3	7	— —	++ —	<i>A. calcoaceticus</i> <i>K. pneumoniae</i> —	10 ⁶ 0	0.10 ≤0.025	excellent	excellent	—	BUN 19→24

* before treatment
after treatment

** UTI: criteria proposed by the UTI Committee
Dr.: doctor's evaluation

CCP: chronic complicated pyelonephritis
CCC: chronic complicated cystitis
BPH: benign prostatic hypertrophy

Table 1-2. Clinical summary of complicated UTI patients treated with pazufloxacin

Patient no.	Age (yr)	Sex	Diagnosis	Catheter (route)	UTI group	Treatment		Symptoms*	Pyuria**	Bacteriuria*			Evaluation**		Side effects	Remarks
			Underlying condition			dose (mg × /day)	duration (days)			species	count	MIC	UTI	Dr.		
19	81	M	CCC	—	G-6	100 × 3	7	++	—	<i>S. epidermidis</i>	10 ⁶ 0	0.78	excellent	excellent	—	
			BPH					—	—	<i>S. saprophyticus</i>		0.78				
			bladder stone					—	—	CNS		12.5				
20	72	F	CCC	—	G-6	200 × 3	5	—	++	<i>E. coli</i>	10 ⁷ 10 ³	0.05	moderate	good	—	
			neurogenic bladder					—	—	<i>E. faecalis</i>		3.13				
			hydronephrosis					—	—	<i>S. epidermidis</i>		100				
21	79	M	CCC	—	G-6	200 × 3	6	++	—	<i>P. aeruginosa</i>	10 ⁷ 10 ⁶	>100	poor	poor	—	
			prostatic cancer					++	—	<i>X. maltophilia</i>		0.78				
			urethral stricture					—	—	<i>P. aeruginosa</i>		100				
22	35	F	CCP	—	/	200 × 3	7	++	++	<i>C. glabrata</i>	10 ³ 0	—	/	excellent	—	
			ureteral stone					—	—	—		—				

* before treatment
after treatment

** UTI: criteria proposed by the UTI Committee
Dr.: doctor's evaluation
BPH: benign prostatic hypertrophy

CCC: chronic complicated cystitis
CCP: chronic complicated pyelonephritis
CNS: coagulase-negative staphylococci

Table 2. Overall clinical efficacy of pazufloxacin in complicated UTI

Bacteriuria \ Pyuria	Cleared	Decreased	Unchanged	Effect on bacteriuria
Eliminated	14	2	1	17 (85.0%)
Decreased				
Replaced	1			1 (5.0%)
Unchanged		1	1	2 (10.0%)
Effect on pyuria	15 (75.0%)	3 (15.0%)	2 (10.0%)	Patient total 20
Excellent	14 (70.0%)		Overall effectiveness 18/20 (90.0%)	
Moderate	4 (20.0%)			
Poor (including failure)	2 (10.0%)			

Table 3. Overall clinical efficacy of pazufloxacin classified by the type of infection

Group		No. of patients (percent of total)	Excellent	Moderate	Poor	Overall effectiveness rate (%)
Monomicrobial infection	group 1 (indwelling catheter)					
	group 2 (post-prostatectomy)					
	group 3 (upper UTI)	5	5			5/5
	group 4 (lower UTI)	8	6	2		8/8
	sub total	13 (65.0)	11	2		13/13 (100)
Polymicrobial infection	group 5 (indwelling catheter)					
	group 6 (no indwelling catheter)	7	3	2	2	5/7
	sub total	7 (35.0)	3	2	2	5/7
Total		20 (100)	14	4	2	18/20 (90.0)

Table 4. Relation between MIC and bacteriological response to pazufloxacin treatment in complicated UTI

Isolates	MIC (μg/ml) Inoculum size 10 ⁶ CFU/ml										Not done	Total
	≤0.39	0.78	1.56	3.13	6.25	12.5	25	50	100	>100		
<i>E. faecalis</i>				2/2	1/1						1/1	4/4
<i>S. agalactiae</i>				0/1								0/1
<i>S. epidermidis</i>		1/1										1/1
<i>S. saprophyticus</i>		1/1										1/1
CNS						1/1						1/1
<i>P. mirabilis</i>	1/1											1/1
<i>E. cloacae</i>	1/1											1/1
<i>E. coli</i>	8/8											8/8
<i>E. aerogenes</i>	1/1											1/1
<i>K. pneumoniae</i>	2/2				1/1							3/3
<i>Klebsiella</i> sp.						1/1						1/1
<i>A. calcoaceticus</i>	1/1											1/1
<i>C. freundii</i>	2/2											2/2
<i>P. aeruginosa</i>										0/1		0/1
<i>X. maltophilia</i>		1/1										1/1
Total (eradication rate %)	16/16 (100)	3/3		2/3	2/2	2/2				0/1	1/1	26/28 (92.9)

No. of strains eradicated/no. of strains isolated CNS: coagulase-negative staphylococci

Table 5. Strains appearing after pazufloxacin treatment in complicated UTI

Isolates	No. of strains* (%)
<i>S. epidermidis</i>	2 (50.0)
<i>E. faecium</i>	1 (25.0)
<i>P. aeruginosa</i>	1 (25.0)
Total	4 (100)
appearing cases/evaluated cases (%)	3/20 (15.0)

* regardless of bacterial count

Table 6-1. Clinical summary of uncomplicated UTI patients treated with pazufloxacin

Patient no.	Age (yr)	Sex	Diagnosis	Treatment		Symptoms*	Pyuria*	Bacteriuria*			Evaluation**		Side effects	Remarks
				dose (mg × /day)	duration (days)			species	count	MIC	UTI	Dr.		
23	43	F	AUP	200 × 3	7	++	+	<i>E. coli</i>	10 ⁵	≤0.025		excellent	—	
						—	—	<i>Pseudomonas</i> sp.	10 ⁴	≤0.025				
24	19	F	AUP	100 × 3	7	—	+	<i>E. coli</i>	10 ⁶	0.05		excellent	—	
						—	—	<i>E. cloacae</i>	10 ⁴	≤0.025				
25	46	F	AUP	200 × 3	7	++	++	<i>E. cloacae</i>	10 ⁵	≤0.025		excellent	—	
						—	—	<i>A. lwoffii</i>	0	0.20				

* before treatment
after treatment

** UTI: criteria proposed by the UTI Committee
Dr.: doctor's evaluation

AUP: acute uncomplicated pyelonephritis

Table 6-2. Clinical summary of uncomplicated UTI patients treated with pazufloxacin

Patient no.	Age (yr)	Sex	Diagnosis	Treatment		Symptoms*	Pyuria*	Bacteriuria*			Evaluation**		Side effects	Remarks
				dose (mg × /day)	duration (days)			species	count	MIC	UTI	Dr.		
26	19	F	AUP	200 × 3	7	++	++	<i>E. cloacae</i>	10 ⁵	≤0.025		excellent	—	
						—	—	<i>S. saprophyticus</i>		0.20				
						—	—	<i>Corynebacterium</i> sp.	10 ⁵	>100				
27	57	F	AUP	200 × 3	6	+	++	<i>Corynebacterium</i> sp.	10 ⁴	0.39		excellent	—	
						—	—	<i>S. agalactiae</i>		100				
						—	—	CNS		0.20				
28	49	M	AUC	200 × 3	5	++	++	<i>E. coli</i>	10 ⁶	≤0.025		excellent	—	
						—	—	<i>E. cloacae</i>		≤0.025				
						—	—	—	0					
29	21	F	AUC	100 × 3	3	++	++	<i>E. coli</i>	10 ⁶	0.05	moderate	excellent	—	
						—	—	NFR	10 ⁵	0.78				
						—	—	—						
30	42	F	AUC	100 × 3	3	++	++	<i>E. faecalis</i>	10 ⁴	3.13	moderate	good	—	
						—	±	NFR		0.20				
						—	—	—	0					
31	72	F	AUC	200 × 3	7	++	++	<i>E. coli</i>	10 ⁶	≤0.025		excellent	—	
						—	—	<i>E. cloacae</i>		≤0.025				
						—	—	NFR	10 ³	3.13				
32	39	M	AUC	200 × 3	7	++	++	<i>E. coli</i>	10 ⁵	≤0.025		good	—	
						—	±	<i>E. cloacae</i>		≤0.025				
						—	—	<i>Serratia</i> sp.		≤0.025				
33	42	M	AUC	200 × 3	7	++	++	<i>E. faecalis</i>	10 ⁶	3.13		excellent	—	
						—	—	<i>E. cloacae</i>		≤0.025				
						—	—	—	0					
34	58	M	AUC	200 × 3	7	++	++	<i>E. coli</i>	10 ⁷	≤0.025		excellent	—	
						—	—	—						
						—	—	—	0					
35	54	F	AUC	200 × 3	7	++	++	<i>K. pneumoniae</i>	10 ⁷	0.05		excellent	—	
						—	—	—						
						—	—	—	0					

* before treatment
after treatment

** UTI: criteria proposed by the UTI Committee
Dr.: doctor's evaluation

AUP: acute uncomplicated pyelonephritis

CNS: coagulase-negative staphylococci
NFR: glucose non-fermentative Gram-negative rod
AUC: acute uncomplicated cystitis

Table 7. Clinical summary of acute prostatitis and epididymitis patients treated with pazufloxacin

Patient no.	Age (yr)	Sex	Diagnosis	Catheter (route)	Treatment		Symptoms*	Pyuria**	Bacteriuria*			Evaluation**		Side effects
			Underlying condition		dose (mg × /day)	duration (days)			species	count	MIC	UTI	Dr.	
36	31	M	acute prostatitis	—	200 × 3	5	++	++	NFR	10 ⁴	3.13	moderate	good	GPT 17→52→22 LAP 174→198→188
			acute epididymitis				—	+	—	0				
			—				—	—	—					
37	20	M	acute epididymitis	—	200 × 3	7	++	++	<i>E. cloacae</i>	10 ⁶	≤0.025		good	—
			—				—	±	<i>X. maltophilia</i>	<10 ³	0.39			
			—				—	—	—					

* before treatment
after treatment

** UTI: criteria proposed by the UTI Committee
Dr.: doctor's evaluation

NFR: glucose non-fermentative Gram-negative rod

常変動は、GPT・LAPの軽度の上昇1例とBUNの上昇1例が認められた。
以上、本剤は尿路感染症に有用な薬剤と考えられた。

文 献

- 1) 熊澤浄一, 小林宏行: 第42回日本化学療法学会総会, 新薬シンポジウム。T-3761, 福岡, 1994

Clinical study of pazufloxacin in urinary tract infections

Masaharu Kan, Kenzo Uema[#] and Susumu Kagawa

Department of Urology, School of Medicine, Tokushima University

2-50-1 Kuramoto-cho, Tokushima 770, Japan

([#] Present address: Department of Urology, Komatsushima Red Cross Hospital)

Makoto Yuasa

Department of Urology, Takamatsu Red Cross Hospital

Pazufloxacin (PZFX) was orally administered to the following patients at a dose of 100~200 mg three times a day after meals for 3~7 days: 22 patients with complicated urinary tract infections, 13 with uncomplicated urinary tract infections, 1 with acute prostatitis and 1 with acute epididymitis. The results were as follows:

- 1) According to the Japanese Urinary Tract Infection (UTI) Drug Evaluation Criteria, the efficacy of PZFX in chronic complicated urinary tract infections was excellent in 14 patients, good in 4, and poor in 2; the overall efficacy rate was 90.0%.
- 2) Bacteriologically, 26 (92.9%) of 28 strains were eradicated in chronic complicated urinary tract infections and all 23 strains were eradicated in acute uncomplicated urinary tract infections.
- 3) As subjective and objective side effects, 1 patient developed nausea. Abnormal findings in clinical tests were mild elevations in GPT, LAP and BUN in 2 patients. These findings indicated that PZFX was effective in treating urinary tract infections.