

外科領域における Cefatrizine の使用経験

川 畑 徳 幸

大阪市立北市民病院外科

白羽弥右衛門・酒井克治・藤本幹夫

上田隆美・平田 智

大阪市立大学外科学第二教室

佐々木 武也

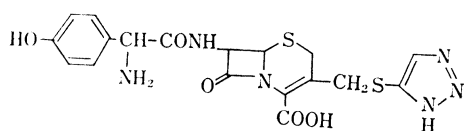
藤井寺市立道明寺病院外科

政 田 明 徳

大阪市城東中央病院外科

Cefatrizine (以下, CFT と略す) は米国プリストル社研究所において開発された新しいセファロsporin系抗生物質で, 下記の構造式をもっており¹⁾, 本剤を経口投与すればよく吸収されて, 体液中で抗菌活性を発揮するといわれている。われわれは本剤を外科領域の疾患に試用したので, その結果をここに報告する。

Chemical structure of CFT



吸収および排泄

健康な成人男子 volunteer 4 例に本剤 250mg ずつを 1 回経口投与して, 血清中濃度および尿中排泄量を測定した。Bioassay には *Sarcina lutea* ATCC 9341 を検定用菌とするカップ法を行ない, analytical standard としては CFT 結晶 Lot No. CM-028, potency 842 μ g/ml を使った。なお, 標準液の希釈には pH 6.4 磷酸緩衝液をもちいた。

1) 血清中濃度: Table 1 左半のように, 血清中の平均濃度は経口投与 30 分後 0.14 μ g/ml, 1 時間後 0.88

μ g/ml, 2 時間後 2.14 μ g/ml, 4 時間後 2.35 μ g/ml となり, 6 時間後でも 1.04 μ g/ml を示した。

2) 尿中排泄量: Table 1 右半のように, 投与 6 時間以内の排泄量は投与量の平均 43% であった。

臨床治療成績

本剤を表在性感染症 42 例を含む 49 例の感染症例 (Table 2) に経口投与し, Table 3 の基準によってその治療効果を判定したが, このなかには小児 3 例が含まれている。投与量は, 原則として成人には 1 日 1g, 小児には 0.5g とし, 毎食後と就寝前の 4 回に分割内服させたが, 症例 47 には 1 日 2g を投与した。投与期間は 2~19 日間, 投与総量は 2~26g である。対象疾患は Table 4 のとおり, フルンケル 6 例, 膿瘍 14 例, 感染粉瘤 3 例, 瘰癧 15 例, 蜂窩織炎 2 例, 化膿性乳腺炎 4 例, 睾丸炎 1 例, 腹腔内膿瘍 1 例, 胆管癌の再発に合併した胆管炎兼術創感染 1 例, 感染性腹壁瘻 1 例, 急性膀胱炎 1 例である。その結果, 49 例中著効 17 例, 有効 15 例, やや有効 10 例, 無効 7 例で, 有効率 85.7% となった。

副作用: 全例に全くみとめられなかった。

考察と総括

CFT の血清中濃度は CEX に比べてやや低く, また

Table 1 Serum level and urinary excretion of CFT after a 250 mg oral administration in four healthy male volunteers

Case No.	Name	Age (yr.)	Body weight (kg)	Serum level (μ g/ml)					Urinary excretion (mg)				
				1/2°	1°	2°	4°	6°	0~2°	2~4°	4~6°	Total	(%)
1	M. T.	33	65	0.28	1.29	2.60	2.48	0.60	15.6	56.0	29.4	101.0	(40.4)
2	T. K.	25	65	trace	0.20	1.24	2.88	1.00	30.4	36.9	32.5	99.8	(39.9)
3	R. O.	39	75	0.3	1.32	1.60	1.72	0.96	20.9	38.0	36.8	95.7	(38.3)
4	N. K.	51	73	trace	0.07	3.12	2.32	1.60	42.0	59.6	32.6	134.2	(53.7)
Average				0.14	0.88	2.14	2.35	1.04	27.2 (10.9)	47.6 (19.1)	32.8 (13.1)	107.6	(43.0)

Table 2 Report of cases treated with CFT

Case No.	Name Age Sex	Diagnosis	Isolated organism MIC ($\mu\text{g/ml}$)	Dosage schedule		Combined surgery	Clinical course and therapeutic response	Side effect	Evaluation
				Dura- g/day (days)	Total dose (g)				
1	Y. K. 25 female	furuncle of face	<i>Staph. epid.</i> (0.39)	1	3	none	On the 3rd day, signs and symptoms of infection disappeared.	none	excellent
2	N. T. 44 male	furuncle of nasal tip		1	3	none	do.	none	excellent
3	T. S. 42 male	furuncle of nose	<i>Staph. aureus</i>	1	9	none	By the 5th day, signs and symptoms subsided.	none	good
4	K. Y. 42 female	furuncle of nasal tip		1	4	none	On the 2nd day, chief signs and symptoms subsided and disappeared by the 4th day.	none	excellent
5	T. K. 32 male	furuncle in lt. anterior chest wall	<i>Staph. epid.</i> (0.78)	1	2	none	On the 2nd day, the core broke out spontaneously, and on the 3rd day pain subsided.	none	excellent
6	Y. J. 34 male	furuncle of face	<i>Staph. aureus</i>	1	7	incision	By the 7th day, all the signs and symptoms disappeared.	none	fair
7	M. T. 4 female	abscess in chin	<i>Staph. aureus</i> (0.39)	0.5	4	incision	On the 3rd day, all the signs and symptoms disappeared.	none	excellent
8	S. O. 47 male	abscess in nape	<i>Staph. epid.</i>	1	3	incision	By the 3rd day, almost all the signs and symptoms disappeared.	none	excellent
9	Y. F. 19 male	abscess of the rt. palm	negative on culture	1	4	incision	On the 3rd day, purulent discharge stopped.	none	excellent
10	B. I. 7 male	abscess in the abdominal wall	<i>Staph. aureus</i>	0.5	7	incision	By the 3rd day, almost all the signs and symptoms disappeared.	none	good
11	Y. S. 28 male	abscess of abdominal wall due to contaminated silk suture		1	7	none	On the 3rd day, signs and symptoms except for redness disappeared.	none	good
12	K. S. 29 male	abscess of abdominal wall	<i>E. coli</i>	1	7	incision	On the 4th day, purulent discharge decreased.	none	good
13	F. S. 37 male	abscess in rt. groin	<i>Staph. aureus</i>	1	6	incision	On the 7th day, signs and symptoms disappeared.	none	good

14	H. T. 33 male	do.	<i>Staph. aureus</i>	1	9	9	incision	By the 7th day, all the signs and symptoms disappeared.	none	fair
15	C. K. 36 female	abscess of rt. labium majus	<i>Staph. aureus</i>	1	7	7	incision	On the 2nd day, pain and redness subsided, and on the 4th day, purulent discharge stopped.	none On the 7th day: GOT 23, GPT 25, LDH 250, ALP 5.0	excellent
16	M. F. 31 male	abscesses in rt. hip and lt. thigh	<i>Staph. aureus</i>	1	5	5	counter incision	On the 3rd day, pain, redness, and purulent discharge disappeared.	none	excellent
17	K. H. 46 male	abscess in rt. hip	<i>Staph. aureus</i>	1	8	8	incision	On the 5th day, signs and symptoms disappeared.	none	good
18	K. N. 60 male	anal abscess	<i>Proteus vul.</i> (3. 12)	1	6	6	incision	On the 3rd day, the signs and symptoms of infection subsided, and by the 7th day all of them disappeared.	none	excellent
19	K. H. 28 male	do.	<i>Staph. aureus</i> (3. 12) <i>Klebsiella</i> (>100)	1	5	5	incision	On the 5th day, pain and purulent discharge disappeared.	none	good
20	T. H. 27 male	do.	<i>Pseudomonas</i> <i>aeruginosa</i>	1	7	7	incision	CFT therapy for 2 weeks could not control contaminated granulation tissue.	none	poor
21	T. I. 29 female	infected atheroma cyst of rt. back	negative on culture	1	3	3	incision	On the 4th day, signs and symptoms of infection subsided, but on the 7th day serous secretion persisted.	none	fair
22	M. S. 65 male	infected atheroma cyst of back	<i>Proteus vul.</i> <i>Staph. epid.</i>	1	8	8	incision reincision 7 days later	By the 7th day, purulent discharge did not subside.	none	poor
23	S. T. 29 male	infected atheroma cyst in rt. hip	negative on culture	1	10	10	incision on the 4th day	In 7 days, pain, redness and swelling subsided, but purulent discharge was not controlled.	none	fair
24	M. U. 46 female	felon of rt. thumb		1	5	5	none	On the 5th day, almost all the signs and symptoms of infection subsided.	none	good
25	K. H. 37 female	felon of lt. thumb	<i>Enterobacter</i>	1	6	6	incision	On the 5th day, almost all the signs and symptoms of infection subsided.	none	good
26	M. E. 26 female	felon of rt. thumb		1	4	4	none	By the 3rd day, pain subsided.	none	excellent

27	K. U. 28 female	felon of rt. index finger	<i>Staph. aureus</i>	1	10	10	incision	On the 7th day, almost all signs of infection were not seen.	none	fair			
28	A. N. 24 female	do.		1	3	3	incision	On the 2nd day, purulent discharge was observed. He was lost because of no visit, but complete healing was expected in a few days.	none	good			
29	K. H. 28 female	do.		1	4	4	incision	Pain and redness disappeared on the 3rd day, but purulent discharge continued 3 days more.	none	good			
30	S. A. 28 female	do.		1	4	4	none	On the 3rd day, all the signs and symptoms of infection subsided.	none	excellent			
31	10 female	felon of lt. middle finger		0.5	4	2	none	On the 5th day, all the signs and symptoms of infection subsided.	none	good			
32	M. A. 63 male	paronychia of rt. middle and ring fingers		1	3	3	none	Pain and redness subsided on the 3rd day, and swelling on the 5th day.	none	excellent			
33	Y. I. 31 male	felon of lt. ring finger		1	4	4	none	On the 4th day, all the signs and symptoms subsided.	none	good			
34	K. K. 25 female	do.		1	4	4	none	On the 3rd day, all the signs and symptoms subsided.	none	excellent			
35	S. N. 30 male	do.		1	4	4	none	On the 4th day, almost all signs and symptoms subsided.	none	excellent			
36	K. M. 23 female	felon of rt. first toe		1	4	4	extraction of nail	On the 4th day, signs and symptoms of infection subsided.	none	good			
37	U. K. 24 female	do.	<i>Staph. aureus</i>	1	7	7	incision and extraction of nail	The infection failed to respond in 7 days, protracting by the 12th day.	none	poor			
38	Y. K. 42 female	do.	<i>Staph. aureus</i>	1	7	7	incision	On the 7th day, all the signs and symptoms of infection subsided.	none	fair			
39	M. K. 30 male	cellulitis of lt. leg	<i>Staph. aureus</i> (0.78)	1	5	5	none	Five days after the onset of infection, the patient referred the clinic with severe complaints. On the 3rd day of CFT treatment, pain, redness, swelling and purulent discharge subsided dramatically.	none	excellent			
40	H. S. 42 male	cellulitis of rt. dorsal foot	Gram negative rod (50.0)	1	6	6	incision	On the 2nd day, pain disappeared, redness and purulent discharge subsided.	none	excellent			

41	M. S. 25 female	rt. purulent mastitis	<i>Staph. aureus</i>	1	14	14	incision on the 4th day	On the 7th day, pain, redness, swelling and local heat disappeared, but purulent discharge continued.	none	fair
42	H. N. 35 female	do.	<i>Staph. aureus</i>	1	10	10	incision	In 7 days of CFT treatment, no relief of complaints was seen.	none	poor
43	N. I. 39 female	do.		1	7	7	none	On the 2nd day, signs and symptoms of infection subsided, and completely disap- peared 3 days later.	none	good
44	I. K. 24 female	lt. purulent mastitis	<i>Staph. aureus</i>	1	4	4	incision	No improvement of infection, necessitating a reincision.	none	poor
45	A. K. 38 male	rt. orchiditis		1	6	6	none	On the 3rd day, only pain subsided.	none	fair
46	S. A. 29 male	intraoperative abscess due to perforated gangraenous appendix		1	7	7	none	In the postoperative course after appende- ctomy, the infection became manifest. On the 2nd day of CFT treatment, the patient became afebrile.	none	good
47	S. T. 46 male	recurrent cancer of gallbladder, purulent cholangitis, infected postoperative wound	<i>Proteus vul.</i> <i>Klebsiella</i> <i>E. coli</i>	2	13	26	two months ago, cholan- giojejunosto- my after Longmire	No marked improvement of infection.	none	poor
48	S. H. 75 female	contaminated sinus of abdominal wall	<i>E. coli</i>	1	19	19	none	After temporary decrease of purulent discharge, the infection recurred.	none	poor
49	K. M. 44 female	acute cystitis	<i>E. coli</i>	1	7	7	none	On the 5th day, irritative signs of bladder reduced, with marked decrease of organi- sms in urine.	none	fair

Table 3 Criteria for evaluating effectiveness of an agent on infectious disease

1. Excellent : The principal symptoms and signs disappear completely within 3 days after onset of the treatment.
2. Good : More than half of the symptoms and signs disappear within 5 days after onset of the treatment.
3. Fair : Any of the symptoms and signs disappears within 7 days after the onset of the treatment.
4. Poor : Either none of the symptoms and signs disappears or their aggravation is observed after 7 days.

Table 4 Clinical results of CFT therapy

Disease	Number of cases	Clinical effect			
		Excellent	Good	Fair	Poor
Furuncle	6	4	1	1	0
Abscess	14	6	5	2	1
Infected atheroma cyst	3	0	0	2	1
Felon	15	5	7	2	1
Cellulitis	2	2	0	0	0
Purulent mastitis	4	0	1	1	2
Orchiditis	1	0	0	1	0
Intraperitoneal abscess	1	0	1	0	0
Contaminated sinus	2	0	0	0	2
Acute cystitis	1	0	0	1	0
Total	49	17	15	10	7
		85.7%			

臓器内濃度もいくぶん低いけれども、多くのグラム陽性球菌やグラム陰性桿菌に対する抗菌力が CEX に比べてはるかに強いとする報告もあるので¹⁾²⁾³⁾⁴⁾、私たちは外科臨床で経験された各種感染症 49 例に本剤を投与し、治療効果を検討した。このなかの表在性感染症は 42 例で、その 37 例 (88.1%) で明らかな効果がみとめられた。したがって、本剤は表在性軟部感染症に対してきわめて有効な薬剤であると考えられる。

本剤の血清中濃度を、まず食後 2 時間を経た volunteer に経口投与して検討し、あわせて胃腸障害発現の有無をも注意深く観察した。その結果、血清中濃度のピークは内服後 4 時間目にえられ、また 6 時間後でもなおかなり有効濃度の持続していることがあきらかになった。しかも食後 2 時間目の内服例中には刺激症状や異和感を訴えたものが全くなかった。食後投与例では空腹時投与例に比べて血中濃度ピークの発現がやや遅れるようであるが、持続時間には差がみられず、尿中排泄量の減少もないことがわかった。さらに、その後の臨床試用例には毎食後と就寝前の 4 回に分割内服させたところ、十分な治療効果がみとめられた。私たちが治療の対象とした症例の大部分は比較的軽症であったので、1日 1g を投与された成人例でも好成績をおさめることができた。しかし重症例にはさらに投与量を増加する必要があるかも知れず、この点は今後の検討にまたねばならない。なお、血液、肝、腎検査等は行っていないが、本剤の経口投与による胃腸障害や、アレルギー性副作用などは全くみとめられなかったから、比較的安全な経口剤であるといえることができる。

む す び

CFT を 49 例の感染症例に投与し、有効率 85.7% の

結果をえた。副作用は全くみられなかった。併せて経口投与後の血清中濃度ならびに尿中排泄量を検討した。本剤は表在性感染症に有効な新抗生物質であると考えられる。

なお、本治験に用いた CFT は萬有製薬(株)から提供されたものである。

文 献

- 1) LEITNER, F.; R. E. BUCK, M. MISIEK, T. A. PURSIANO & K. E. PRICE: BL-S 640, a cephalosporin with a broad spectrum of antibacterial activity: Properties *in vitro*. *Antimicrob. Agents & Chemoth.* 7: 289~305, 1975
- 2) LEITNER, F.; D. R. CHISHOLM, Y. H. TSAI, G. E. WRIGHT, R. G. DEREGIS & K. E. PRICE: BL-S640, a cephalosporin with a broad spectrum of antibacterial activity: bioavailability and therapeutic properties in rodents. *Antimicrob. Agents & Chemoth.* 7: 306~310, 1975
- 3) WATANAKUNAKORN, C.; T. BANNISTER & C. GLOTZBECKER: Susceptibility of clinical isolates of enterobacteriaceae to BL-S640, a new oral cephalosporin. *Antimicrob. Agents & Chemoth.* 7: 381~385, 1975
- 4) YOURSSOWSKY, E.; E. SCHOUTENS & M. P. VANDERLINDEN: Comparative inhibitory activity of BL-S 640 and two other cephalosporins. *J. Antibiotics* 28: 590~593, 1975

CLINICAL STUDIES ON CEFATRIZINE
IN THE FIELD OF SURGERY

NORIYUKI KAWABATA

Department of Surgery, Osaka City Kita Hospital

YAEMON SHIRAHA, KATSUJI SAKAI, MIKIO FUJIMOTO,

TAKAMI UEDA and SATORU HIRAO

Department of Surgery, Osaka City University Medical School

TAKEYA SASAKI

Department of Surgery, Domyoji Hospital, Fujiidera City

AKINORI MASADA

Department of Surgery, Jotochuo Hospital, Osaka City

Cefatrizine (CFT) was given for acute cases of infections mainly in soft tissues, and effective responses were seen on 42 of all 49 patients. In addition the serum level and urinary excretion were investigated using a bioassay procedure.

Cefatrizine is a promising antibiotic highly effective for acute infections in the field of surgery without any untoward side effect.