WELL-CONTROLLED COMPARATIVE STUDY OF CEFROXADINE AND A LONG-ACTING PREPARATION OF CEPHALEXIN IN ACUTE SKIN INFECTION

Jirô Arata and Yasuo Yamamoto
Department of Dermatology, Kochi Medical School

Katsuyuki Takeda and Takashi Oguni
Department of Dermatology, School of Medicine, Tokushima University

Yoshiharu Miki and Satoshi Shiraishi
Department of Dermatology, Ehime University School of Medicine

Kenzo Arakawa
Department of Dermatology, Sumitomo Besshi Hospital

Mitsukuni Enomoto and Seiji Arase
Department of Dermatology, Kochi Prefectural Central Hospital

Tomomichi Fujita
Department of Dermatology, Kochi Red Cross Hospital

Taneo Harada
Department of Dermatology, Anan Kyoei Hospital

Akira Kuwabara
Department of Dermatology, Ehime Prefectural Central Hospital

Atsuki Kondo
Department of Dermatology, Kochi Municipal Citizen Hospital

Takashi Nakakita and Naohiro Kashiwa
Department of Dermatology, Takamatsu Red Cross Hospital

Takashi Nagai
Department of Dermatology, Yashima Sougo Hospital

Noboru Ohkuma
Department of Dermatology, Mitoyo Sougo Hospital

Kazuo Saito
Department of Dermatology, Tokushima Citizen Hospital

Sadaaki Sagawa
Department of Dermatology, Komatsushima Red Cross Hospital

Tadatoshi Yamamoto
Department of Dermatology, Tokushima Prefectural Central Hospital

Controller

YUKITOSHI FUJITA
Department of Urology, Kochi Medical School

Analyst

TAICHI KARIYA
Department of Statistics, Kawasaki Medical School

(Received December 1, 1981)

A multicenter well-controlled comparative study of cefroxadine and a long-acting preparation of cephalexin (L-cephalexin) was performed. Patients admitted to the present study were limited to the following diseases: furuncle, furunculosis, carbuncle, folliculitis (except acne), cellulitis and lymphangitis. The patients were over 12 years of age and weighed more than 25 kg.

Cefroxadine was administered in capsules at the dosage of 250 mg two times a day after meals in the morning and in the evening. Cephalexin was given in granules prepared for longer action (L-cephalexin) at the dosage of 500 mg two times a day after meals in the morning and evening. No patient was treated longer than 8 days. Each drug was packed to fill a course of 7 day treatment. Pain, redness and edema were the main symptoms checked. The total number of patients was 99 ; 52 for cefroxadine and 47 for L-cephalexin. One patient in the cefroxadine group and 5 in the L-cephalexin group were excluded. There were 3 dropouts each in the cefroxadine and L-cephalexin group. Thus, 87 patients, 48 on cefroxadine and 39 on L-cephalexin, were submitted to clinical evaluation. Side effects were analyzed in 93 patients, 49 on cefroxadine and 44 on L-cephalexin.

The overall efficacy was evaluated subjectively by attending doctors. Taking into consideration the time needed for marked improvement and the severity of the disease, the attending doctors graded the results as excellent, good, fair or poor. Patients evaluated as better than "good" were 39 of 48(81.3%) for cefroxadine and 32 of 39(82.1%) for L-cephalexin. The difference between the two drugs was not statistically significant.

In evaluation of the degree of improvement on each follow-up day, we found no statistically signifficant difference between the two drugs as to any grade of improvement on any evaluation day.

Evaluation was partially standardized, by totalling the difference of points for pain, redness, and edema, which were calculated by subtracting the grade number on each observation day from the grade number at the first visit. No statistically significant difference between the two drugs were found as to any grade of effectiveness on any evaluation day.

A patient on L-cephalexin complained of a feeling of thirst. No other side effect was observed in either group of the drugs.

In conclusion, cefroxadine 250 mg two times a day was considered to be as effective as L-cephalexin 500 mg two times a day against acute skin infections.

In a previous paper we reported the result of a multicenter well-controlled double-blind test of cefroxadine and cephalexin, showing that cefroxadine 250 mg two times a day and cephalexin 250 mg four times a day were equally effective in the management of acute skin infections[1]. On the basis of this result we have performed a multicenter well-controlled comparative study of cefroxadine and a long-acting preparation of cephalexin (L-cephalexin). This paper reports the result of this controlled study.

MATERIALS AND METHOD

1. Patients

Patients admitted to the present study were limited to the following diseases: furuncle, furunculosis, carbuncle, folliculitis (except acne), cellulitis and lymphangitis. The patients were over 12 years of age and weighed more than 25 kg. Pregnant or suckling women, patients allergic to PCs and/or CEPs, patients with severe hepatic or renal disorders or patients who were on other antimicrobial agents, were excluded from the present study.

2. drugs

Cefroxadine was administered in capsules at the dosage of 250 mg two times a day after meals in the morning and in the evening. Cephalexin was given in granules prepared for longer action at the dosage of 500 mg two times a day after meals in the morning and in the evening. Each drug was packed to fill a course of 7 day treatment. Packs of each drug were allocated randomly in a set of 2 packs each of cefroxadine and L-cephalexin. These four packs per set were numbered 1 to 4 and each pack was prescribed according to the number in order of visit of patients. The key codes of each pack and set were kept by the controller of this study until key opening. Drugs, picked out randomly by the controller, were checked before and after the present study at Kyoto Pharmaceutical college.

Incision and drainage were restricted to the minimum. Combination with other antimicrobial, systemic or topical, and antiinflammatory drugs were to be avoided. No patient was treated longer than 7 days.

3. Follow-up of the patients and method of evaluation

The patients on the treatment were followed up for symptoms and side effects on the third, fifth and seventh day. Pain, redness and edema were the main symptoms checked. Microbiological examination was done when possible before the treatment, and MIC of the isolates were tested at Tokyo Sogo Rinsho Kensa Center following the standardized method of the Japanese Society for Chemotherapy.

The overall efficacy was evaluated subjectively by attending doctors and the results were graded as excellent, good, fair or poor.

Attending doctors also evaluated the degree of improvement on each follow-up observation day as markedly improved, improved, slightly improved and not changed. Usefulness of the drug concerned was evaluated by attending doctors as excellent, satisfactory, good, dissatisfactory, and very dissatisfactory.

The evaluation of the efficacy was standardized partially by totalling the differences of points for pain, redness, and edema, which were calculated by subtracing the grade number on each observation day from the grade number at the first visit. Pain, redness, and edema were respectively graded as 3 at the first visit. The degree of an absent symptom was graded as 0. The follow-up grading was done in comparison of the grades at the first visit as follows: no improvement, 3; slightly improved, 2; improved, 1; and disappearance of the symptom, 0. If a symptom was aggravated, the corresponding grade number was marked with a double circle, and on evaluation we subtracted 1 point from the total score. Total scores and the corresponding evaluations are shown in Table 1.

Patients who dropped out were indicated prior to key opening, if any of the following occurred; major protocol deviation, drug was discontinued due to side effects early in the course of the treatment, key code of the case concerned was opened

Table 1 Evaluation of efficacy by total score

Efficacy \ No. of symptoms*	3	2	1
Excellent	9-8	6	3
Good	7-5	5-4	2
Fair	4-2	3-2	1
Poor	1-0	1-0	0

* redness, pain, edema

Table 2 Number of patients admitted to the analysis

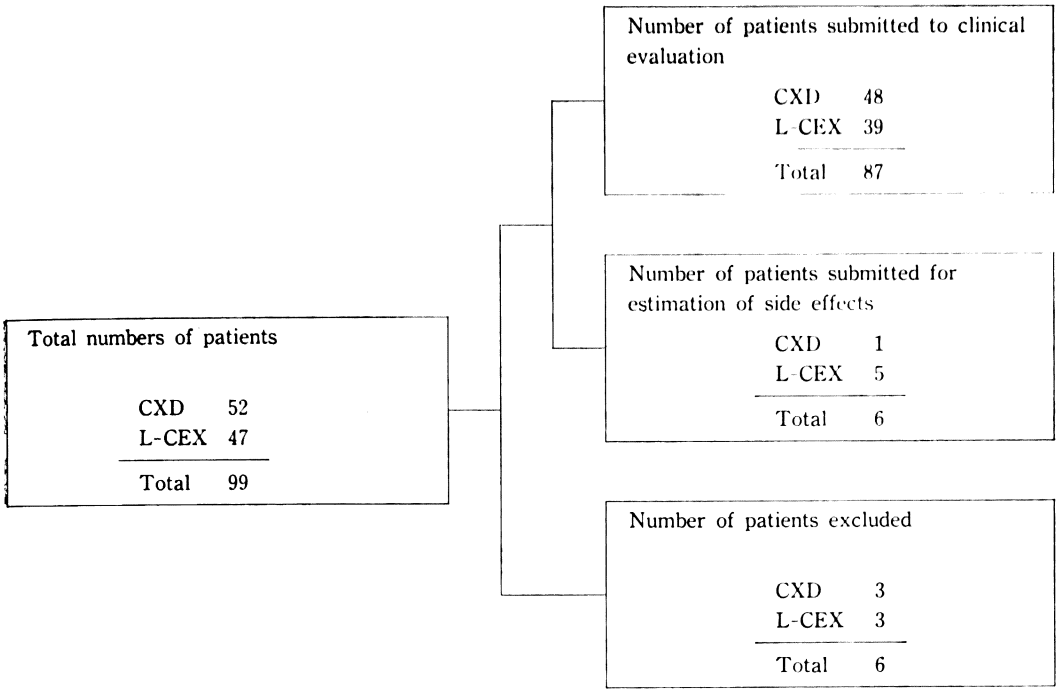


Table 3 Exclusion and drop-out

Reason for drop-out	CXD	L-CEX	Total
Used in disease not indicated	1	4	5
Combined use of analgesics or anti-inflammatory drugs	0	1	1
Total	1	5	6
Reason for exclusion	CXD	L-CEX	Total
Not followed up	3	3	6

before the final blind evaluation, test drug was administered in combination with other drugs which might influence the course of the disease concerned, or there was anything which was judged as inappropriate for the present study by the evaluation committee.

RESULTS AND STATISTICAL ANALYSIS

Table 2 shows the number of patients admitted to the analysis. The total number of patients was 99, 52 for cefroxadine and 47 for L-cephalexin. One patient in the cefroxadine group and 5 in the L-cephalexin group were excluded. There were 3 dropouts each in cefroxadine group and L-cephalexin group. Thus, 87 patients, 48 on cefroxadine and 39 on L-cephalexin, were submitted to clinical evaluation. Side effects were analyzed in 93 patients, 49 on cefroxadine and 44 on L-cephalexin. Reasons for exclusion and drop-out are shown in Table 3. Statistical analysis of patients' characteristics showed no significant difference between the two drug groups (Table 4).

The overall efficacy evaluated subjectively by attending doctors (Table 5): Patients evaluated as excellent were 17 of 48 (35.4%) in the cefroxadine group and 18 of 39 (46.2%) in the cephalexin group; total patients evaluated as better than

Table 4 Patient characteristics in each treatment group

Characteristics		CXD	L-CEX	Statistical test
Sex	Male	31	20	$\chi^2=2.294$ N.S.
	Female	18	24	
Age	~ 30	19	16	t =1.157 N.S.
	31 ~ 50	19	10	
	51 ~	11	18	
Body weight (kg)	~ 50	11	12	t =0.095 N.S.
	51 ~ 60	23	16	
	61 ~	15	16	
Diagnosis	Folliculitis	10	9	$\chi^2=1.878$ N.S.
	Furuncle	22	18	
	Furunculosis	8	5	
	Carbuncle	1	2	
	Cellulitis	3	1	
	Lymphangitis	4	5	
	Others	1	4	
Maturity of lesion	Immature	10	13	$\chi^2=1.506$ N.S.
	Mature	27	19	
	Mixed	3	2	
	Unknown	9	10	
Severity	Severe	4	4	$\chi^2=1.365$ N.S.
	Moderate	39	28	
	Mild	6	12	
Associated disease	Absent	39	30	$\chi^2=3.096$ N.S.
	Skin disease	10	12	
	Others	0	2	
Period from the onset to start of medication	1	1	1	t =0.793 N.S.
	2	9	11	
	3	13	14	
	4	8	3	
	5	8	6	
	6	2	2	
	7	3	3	
	8 ~	5	4	
Minor surgical intervention	None	32	29	$\chi^2=0.399$ N.S.
	Incision	12	9	
	Drainage	5	6	
Combined drugs	Absent	46	42	$\chi^2=1.919$ N.S.
	Present	3	2	
Isolated organism	*S. aureus*	16	19	$\chi^2=5.837$ N.S.
	S. epidermidis	6	5	
	Mixed infection	6	2	
	Others	7	3	

Table 5 Overall clinical efficacy by attending doctors

Drug \ Efficacy	Excellent	Good	Fair	Poor	Total	Statistical test
CXD	17 (35.4%)	22 (81.3%)	7 (95.8%)	2 (100.0%)	48	t = 0.731 χ^2 = 0.033 N.S.
L-CEX	18 (46.2%)	14 (82.1%)	4 (92.3%)	3 (100.0%)	39	

Table 6 Follow-up degree of improvement evaluated by attending doctors

Drugs \ Degree of improvement		Markedly improved	Improved	Slightly improved	Not changed	Total	Statistical test
3rd day	CXD	15 (34.1%)	15 (68.2%)	8 (86.4%)	6 (100.0%)	44	t = 0.058 χ^2 = 0.000 N.S.
	L-CEX	14 (36.8%)	11 (65.8%)	8 (86.8%)	5 (100.0%)	38	
5th day	CXD	12 (46.2%)	10 (84.6%)	4 (100.0%)	0	26	t = 0.421 N.S. P = 0.836 FISHER
	L-CEX	11 (50.0%)	9 (90.9%)	2 (100.0%)	0	22	
7th day	CXD	20 (66.7%)	8 (93.3%)	2 (100.0%)	0	30	t = 0.873 N.S. P = 0.862 FISHER
	L-CEX	12 (54.6%)	8 (90.9%)	1 (95.5%)	1 (100.0%)	22	

Table 7 Usefulness

Drug \ Usefulness	Excellent	Satisfactory	Good	Un-satisfactory	Very un-satisfactory	Total	Statistical test
CXD	12 (24.5%)	23 (71.4%)	11 (93.9%)	2 (97.9%)	1 (100.0%)	49	t = 1.006 χ^2 = 0.032 N.S.
L-CEX	15 (38.5%)	15 (76.9%)	6 (92.3%)	3 (100.0%)	0	39	

"good" were 39 of 48 (81.3%) for cefroxadine and 32 of 39 (82.1%) for cephalexin. Though the rate of "excellent" was higher in L-cephalexin, the difference between the two drugs was not statistically significant.

Table 6 shows the evaluation of the degree of improvement on each follow-up observation day by attending doctors. We found no statistically significant difference between the drugs as to any grade of improvement on any evaluation day.

The evaluation of usefulness is shown in Table 7. Results better than "satisfactory" were obtained in 72.9% of cefroxadine patients and in 76.9% of L-cephalexin group. The difference in usefulness between the two drugs was not statistically significant.

The results of the partially standardized evaluation are presented in Table 8. On the 3rd day, 61.4% in the cefroxadine group and 60.5% in the L-cephalexin group were better than "good". On the 5th day, 88.5% of patients on cefroxadine and 81.8% of patients on L-cephalexin showed a result better than "good". On the 7th day the results were better than "good" in 93.3% for cefroxadine

Table 8 Partially standardized clinical evaluation

Drugs \ Efficacy		Excellent	Good	Fair	Poor	Total	Statistical test
3rd day	CXD	9 (20.5%)	18 (61.4%)	11 (86.4%)	6 (100.0%)	44	t =0.044 χ^2=0.022 N.S.
	L-CEX	9 (23.7%)	14 (60.5%)	9 (84.2%)	6 (100.0%)	38	
5th day	CXD	11 (42.3%)	12 (88.5%)	1 (92.3%)	2 (100.0%)	26	t =0.293 N.S. P =0.806 FISHER
	L-CEX	9 (40.9%)	9 (81.8%)	2 (90.9%)	2 (100.0%)	22	
7th day	CXD	20 (66.7%)	8 (93.3%)	1 (96.7%)	1 (100.0%)	30	t =0.924 N.S. P =0.705 FISHER
	L-CEX	12 (54.6%)	7 (86.4%)	3 (100.0%)	0	22	

and in 86.4% for cephalexin. The difference between the two drugs were not statistically significant as to any grade of effectiveness on any evaluation day.

Evaluation of each of the main symptoms checked is shown in Table 9. There was no statistically significant difference as to any sumptom on any evaluation day except the rate of marked improvement of edema on the 7 th day.

As shown in Table 10 a patient on L-cephalexin complained of a feeling of thirst. No other side effect was observed in either group of the drugs.

Analyses were stratified according to sex, age, diagnosis, severity of the disease, associated disease, minor surgical interventions such as drainage or incision, and isolated organisms. As shown in Table 11, there were no statistically significant differences except usefulness ($P<0.05$) in the age group under 30 years where L-cephalexin was superior.

Minimum inhibitory concentrations(MICs) of cefroxadine and cephalexin against *Staphylococcus aureus* and *Staphylococcus epidermidis* isolated from patients in the present study were shown in Table 12. At the inoculum size of 10^6 CFU/ml, 6 of 35 strains of *Staphylococcus aureus* showed MIC of 50 μg/ml or more of both cefroxadine and cephalexin. At 10^6 CFU/ml these 6 strains were inhibited at the concentration of 6.25 μg/ml or more. MICs against *Staphylococcus epidermidis* were lower than those against *Staphylococcus aureus* by one or two dilutions. Cefroxadine and cephalexin showed almost the same MICs at 10^6 CFU/ml. At 10^6 CFU/ml, MICs of cefroxadine were slightly lower against sensitive strains of *Staphylococcus aureus*.

DISCUSSION

Our previous study[1] compared cefroxadine 250 mg two times a day and cephalexin 250 mg four times a day in the management of acute bacterial skin infection, showing that there was no statistically significant difference between the two drug groups. On the basis of this previous study we performed a multicenter well-controlled study between cefroxadine 250 mg two times a day and a long-acting preparation of cephalexin 500 mg two times a day in the treatment of acute skin infection. We found no statistically significant difference.

The long-acting preparation of cephalexin used in the present study is composed at the rate of 3 to 7 of granules soluble in the stomach and of those soluble in the intestine and, taken after meals, the serum concentration[2] rises and lowers gradually over a period of 12 hours with a plateau-like curve, while its peak is about half of that of conventional preparations of cephalexin. UEDA et al[3] showed cefroxadine and conventional cephalexin followed a similar serum concentration curve over a period of 6 hours after oral administration to healthy volunteers. Thus, it is considered that cefroxadine 250 mg yields a peak level of serum

Table 9 Improvement of the main symptoms checked

Symptom	Day	Improvement / Drug	+++	++	+	−	×	Total	Statistical test
Pain	3rd day (%)	CXD	17 (40.5)	16 (78.6)	5 (90.5)	3	1	42	t =0.408 χ^2 = 0.602 N.S.
		L-CEX	15 (39.5)	11 (68.4)	10 (94.7)	1	1	38	
	5th day (%)	CXD	18 (75.0)	4 (91.7)	2 (100.0)	0	0	24	t =0.157 P =0.676 FISHER N.S.
		L-CEX	16 (72.7)	4 (90.9)	2 (100.0)	0	0	22	
	7th day (%)	CXD	24 (85.7)	3 (96.4)	1 (100.0)	0	0	28	t =0.674 P =0.880 FISHER N.S.
		L-CEX	17 (77.3)	5 (100.0)	0	0	0	22	
Redness	3rd day (%)	CXD	4 (9.1)	15 (43.2)	19 (86.4)	5	1	44	t =0.520 χ^2 =0.400 N.S.
		L-CEX	5 (13.2)	15 (52.6)	11 (81.3)	6	1	38	
	5th day (%)	CXD	5 (19.2)	16 (80.8)	3 (92.3)	2	0	26	t =0.173 P =0.958 FISHER N.S.
		L-CEX	6 (27.3)	11 (77.3)	2 (86.4)	3	0	22	
	7th day (%)	CXD	10 (33.3)	18 (93.3)	0 (93.3)	2	0	30	t =0.181 P =0.862 FISHER N.S.
		L-CEX	7 (31.8)	13 (90.9)	1 (95.5)	1	0	22	
Edema	3rd day (%)	CXD	11 (26.8)	15 (63.0)	8 (82.9)	6	1	41	t =0.815 χ^2 =1.715 N.S.
		L-CEX	9 (27.3)	6 (45.5)	12 (81.8)	4	2	33	
	5th day (%)	CXD	10 (41.7)	11 (87.5)	1 (91.7)	2	0	24	t =0.671 P =0.446 FISHER N.S.
		L-CEX	7 (36.8)	7 (73.7)	3 (89.5)	2	0	19	
	7th day (%)	CXD	20 (71.4)	6 (92.9)	1 (96.4)	1	0	28	t =1.659 P <0.1 P =0.724 FISHER
		L-CEX	10 (47.6)	8 (87.5)	1 (90.5)	2	0	21	

+++ : Disappeared, ++ : Improved, + : Slightly improved, − : Not improved, × : Aggravated

Table 10 Side effect

Drugs	Absent	Present		Ratio (%)	Statistical test
		Continued	Discontinued		
CXD	49	0	0	0/49 (0)	P=0.946 FISHER N.S.
L-CEX	43	1*	0	1/44 (2.3)	

*: Feeling of thirst

Table 11-1 Results of stratified analysis

Strata		No. of patients CXD	No. of patients L-CEX	Overall clinical efficacy* (better than "good") 20 40 60 80(%)	Statistical test W test	Statistical test χ^2 test	No. of patients CXD	No. of patients L-CEX
Sex	Male	30	18		t 0.543 N.S.	P=0.707 Fisher	21	7
	Female	18	21		t 0.423 N.S.	P=0.884 Fisher	9	15
Age	~30	18	14		t 1.772 P<0.1	P=0.875 Fisher	10	4
	31~50	19	9		t 0.056 N.S.	P=0.969 Fisher	14	6
	51~	11	16		t 0.547 N.S.	P=0.765 Fisher	6	12
Diagnosis	Folliculitis	10	9		t 0.621 N.S.	P=0.916 Fisher	7	3
	Furuncle Furunculosis Carbuncle Cellulitis	31	25		t=0.706 N.S.	χ^2=0.009 N.S.	21	17
	Lymphangitis	7	5		t=0.648 N.S.	P=0.833 Fisher	2	2
Severity	Mild	5	11		t=1.305 N.S.	P=0.706 Fisher	1	7
	Moderate	31	18		t=0.170 N.S.	χ^2=0.090	24	11
	Severe	3	3		t=0.000 N.S.	P=0.429 Fisher	3	1
Associated disease	Absent	31	22		t=0.638 N.S.	χ^2=0.099	25	12
	Skin disease	8	8		t=0.203 N.S.	P=0.582 Fisher	3	5
	Others	—	2		—	—	—	2
Drainage or incision	None	27	26		t=0.888 N.S.	P=0.543 Fisher	19	11
	Drainage	2	3		t=0.282 N.S.	P=0.789 Fisher	2	4
	Incision	10	3		t=0.112 N.S.	P=0.524 Fisher	7	4
Isolated organism	*S. aureus*	12	14		t=0.649 N.S.	P=0.835 Fisher	7	9
	S. epidermidis	5	3		t=0.847 N.S.	P=0.667 Fisher	4	2
	Mixed infection	6	0		t=1.350 N.S.	P=0.286 Fisher	4	1
	Others	6	2		t=0.493 N.S.	P=0.933 Fisher	5	1

* : By attending doctors ●——● : CXD

** : Partially standardized (up to 7th day) ×-----× : L-CEX

Table 11-2 Results of stratified analysis

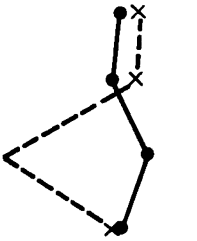
Clinical efficacy** (better than "good") 20 40 60 80(%)	Statistical test W-test	Statistical test χ^2 test	No. of patients CXD	No. of patients L-CEX	Usefulness (better than "satisfactory") 20 40 60 80(%)	Statistical test W-test	Statistical test χ^2-test
	t =1.301 N. S.	P =0.500 Fisher	30	18		t 0.457 N. S.	χ^2 0.000 N. S.
	t =0.559 N. S.	P =0.972 Fisher	18	21		t 0.927 N. S.	P =0.937 Fisher
	—		18	14		t 2.133 P<0.05	P =0.306 Fisher
	t =-0.046 N. S.	P =0.958 Fisher	19	9		t =0.368 N. S.	P 0.969 Fisher
	t =1.178 N. S.	P =0.539 Fisher	11	16		t =0.000 N. S.	P =0.829 Fisher
	t =0.986 N. S.	P =0.933 Fisher	10	9		t =1.379 N. S.	P =0.916 Fisher
	t =0.862 N. S.	P =0.838 Fisher	31	25		t =0.376 N. S.	χ^2 =0.045
	—		7	5		t =0.086 N. S.	P 0.727 Fisher
	—	P =0.891 Fisher	5	10		t =0.552 N. S.	P 0.809 Fisher
	—	P =0.045 Fisher	27	18		t =0.639 N. S.	χ^2 0.002
	—	P =0.500 Fisher	3	2		t =0.000 N. S.	P =1.000 Fisher
	t =0.505 N. S.	P =0.877 Fisher	28	21		t =0.793 N. S.	χ^2 =0.007
	t =0.207 N. S.	P =0.558 Fisher	7	7		t =0.409 N. S.	P =0.628 Fisher
	—	—	—	2		—	
	t =0.023 N. S.	P =0.766 Fisher	24	24		t =1.472 N. S.	χ^2 =0.506
	—	P =0.939 Fisher	2	3		t =0.455 N. S.	P =0.944 Fisher
	t =0.414 N. S.	P =0.452 Fisher	9	3		t =0.114 N. S.	P =0.524 Fisher
	t =1.011 N. S.	P =0.931 Fisher	11	14		t =1.117 N. S.	P =0.835 Fisher
	—	P =0.905 Fisher	4	3		t =0.000 N. S.	P =0.667 Fisher
	—	P =0.800 Fisher	5	0		t =1.058 N. S.	P =0.571 Fisher
	t =0.558 N. S.	P =0.286 Fisher	5	2		t =0.734 N. S.	P =0.583 Fisher

Table 12 Susceptibility of *S.aureus* and *S.epidermidis*

1) *S. aureus* 35 strains (Inoculum size 10^8 CFU/ml)

Drug \ MIC	<0.19	0.19	0.39	0.78	1.56	3.13	6.25	12.5	25	50	100	>100μg/ml
CXD					4	16	6	3		3	1	2
CEX					5	15	5	4		3		3

(Inoculum size 10^6 CFU/ml)

Drug \ MIC	<0.19	0.19	0.39	0.78	1.56	3.13	6.25	12.5	25	50	100	>100μg/ml
CXD				3	12	12	2	2	2	1	1	
CEX				2	7	16	4	2	1	1	2	

2) *S. epidermidis* 11 strains (Inoculum size 10^8 CFU/ml)

Drug \ MIC	<0.19	0.19	0.39	0.78	1.56	3.13	6.25	12.5	25	50	100	>100μg/ml
CXD				5	4			1			1	
CEX				5	4			1			1	

(Inoculum size 10^6 CFU/ml)

Drug \ MIC	<0.19	0.19	0.39	0.78	1.56	3.13	6.25	12.5	25	50	100	>100μg/ml
CXD			3	6		1			1			
CEX			1	7	1	1			1			

concentration as high as L-cephalexin 500 mg and that the duration of active concentration of cefroxadine is half as long as that of L-cephalexin.

TOKUDA et al[4] and we showed that in rabbits[4] and rats[5] the skin concentration after oral administration was maintained longer in the cefroxadine group than in the conventional cephalixin group. KOBAYASHI et al[6] also confirmed that in rabbits, the serum concentration of cefroxadine was more long-acting with a lower peak level than that of cephalexin. These facts could be explained, in part by the difference of species, but also shows that something is different in pharmacokinetics between the two drugs.

Our experiments in golden hamsters[7] showed that the effectiveness of an antibiotic against experimentally induced staphylococcal skin infection does not always rise with increases of the daily frequencies of administration. Skin repair activity seems higher than the repair activity of other tissues, and an antibiotic could produce a good clinical effect at a lower concentration than the MIC against a causative organism, by static action to help the repairing process if the host repairing mechanism is normal

On the basis of these considerations we were able to explain the result of the present study, which confirmed our previous double-blind study[1].

REFERENCE

1) ARATA, J. et al: Double blind Test of Cefroxadine (CGP-9000) vs Cephalexin in acute skin infection, Chemotherapy (Tokyo), 28 : 1070～1081, 1980
2) MAEKAWA, H. et al: Cephalexin preparation with prolonged activity Jpn. J. Antibiotics, 30 : 631～638, 1977
3) UEDA, Y. et al: Clinical studies on Cefroxadine(CGP-9000), Chemotherapy (Tokyo) 28 (S-3) : 194～204, 1980
4) TOKUDA, Y. et al: Basic and clinical studies of Cefroxadine (CGP-9000) in the treatment of pyoderma, Chemotherapy (Tokyo) 28 (S-3) : 515～520, 1980
5) YAMAMOTO, Y. et al: Fundamental studies on Cefroxadine (CGP-9000), Chemotherapy (Tokyo) 28(S-3) : 92～97, 1980
6) KOBAYASHI, Y. et al: Fundamental studies on Cefroxadine (CGP-9000), Chemotherapy (Tokyo), 28(S-3) : 92～97, 1980
7) ARATA, J. et al: In preparation

急性皮膚感染症に対する Cefroxadine と持続性 Cephalexin の比較臨床試験 (well-controlled study)

荒田次郎・山本康生
高知医科大学皮膚科学教室

武田克之・小国隆
徳島大学医学部皮膚科学教室

三木吉治・白石聰
愛媛大学医学部皮膚科学教室

荒川謙三
住友別子病院皮膚科

榎本充邦・荒瀬誠治
高知県立中央病院皮膚科

藤田知道
高知赤十字病院皮膚科

原田種雄
阿南共栄病院皮膚科

桑原章
愛媛県立中央病院皮膚科

近藤厚樹
高知市立市民病院皮膚科

中北隆・柏尚裕
高松赤十字病院皮膚科

永井隆
屋島総合病院皮膚科

大熊登
三豊総合病院皮膚科

斎藤一夫
徳島市民病院皮膚科

佐川禎昭
小松島赤十字病院皮膚科

山本忠利
徳島県立中央病院皮膚科

コントローラー

藤田幸利
高知医科大学泌尿器科学教室

解 析 担 当

仮 谷 太 一

川崎医科大学統計学

急性皮膚感染症に対する Cefroxadine (CXD) と持続性 Cephalexin (L-CEX) の比較臨床試験を well-controlled 法によって実施した。

投与量は，CXD 1日 250 mg を2回，L-CEX 1日 500 mg を2回，朝，夕食後経口投与とし，投与日数は最高7日間とした。その結果は以下のとおりであった。

総症例は CXD 投与群 52 例，L-CEX 投与群 47 例，計 99 例であり，そのうち臨床評価例数は CXD 群 48 例，L-CEX 群 39 例，計 87 例であった。

主治医による総合効果では，有効以上 CXD 群 39/48(81.3%)，L-CEX 群 32/39(82.1%) で両群間に有意差は認められなかった。また，主要症状（疼痛，発赤，浮腫範囲）の改善度による点数化効果判定では，有効以上は CXD 群 61.4%(3日目)，88.5%(5日目)，93.3%(7日目) で，L-CEX 群 60.5%(3日目)，81.8%(5日目)，86.4%(7日目) となり，いずれにおいても有意差は認められなかった。

副作用は L-CEX 群に1例（口渇感）が認められたのみで，その他の副作用は，両群とも認められなかった。

以上の結果から，中等症以下の急性皮膚感染症の治療において CXD 1日 250 mg 2回と L-CEX 1日 500 mg 2回とは同等の効果を発揮し得ると考えられた。