

外科領域における Bacampicillin の使用経験

政田明德・北野福男

城東中央病院外科

酒井克治・藤本幹夫・平尾 智・上田隆美

大阪市立大学医学部第二外科学教室

土居 進

大阪市立北市民病院外科

沢田 晃

大阪市立桃山市民病院外科

佐々木武也・前田貞邦

藤井寺市立道明寺病院外科

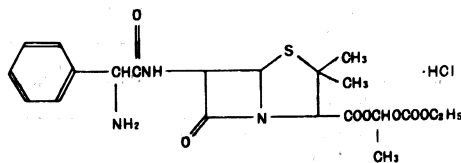
川畑徳幸・白羽弥右衛門

芦原病院外科

Bacampicillin (以下 BAPC と略記) はスウェーデンのアストラ社研究所において開発された新しい合成ペニシリンで、Fig.1のような構造式をもっており、経口投与により加水分解されて Ampicillin となり、強い抗菌力を示す。また本剤はAmpicillinよりも吸収がよいのが特徴とされている¹⁾。

われわれは本剤を外科領域の感染症例に試用したので、その結果をここに報告する。

Fig.1 Chemical structure of BAPC



臨床治療成績

本剤を外科領域の感染症43例 (Table 1) に経口投与し、Table 2の基準に従って、その治療効果を著効、有効、やや有効あるいは無効と判定した。対象疾患はTable 3のとおり、癰およびよう6例、感染粉瘤6例、陰囊皮下膿瘍および肛門周囲膿瘍6例、癰疽5例、蜂巣炎7例、骨髄炎2例、急性胆嚢炎1例、虫垂穿孔性腹膜炎2例、術後創感染症5例および感染瘻孔3例である。

投与量としては1回量を ABPC 力価として 250mg あるいは 500mg とし、1日3ないし4回経口投与した。1日3回投与の場合は毎食後に投与し、4回投与の場合は毎食後と就寝前に投与することとした。投与期間は3～23日間で、投与総量は2.25～18g、平均10.5gであった。その結果、43例中著効8例、有効22例、やや有効6例、無効7例で、著効+有効=有効率69.8%となった。

また病巣から菌が分離された33例について細菌学的効果と臨床効果とを比較したところ、Table 4のように菌の消失した症例が22例 (70%) あり、これらの症例のなかで著効あるいは有効例とみなされた症例数は20例 (有効率78.5%) であって、細菌効果と臨床効果がよく相関していた。

副作用

症例35では1日量として1gを1日間投与、その翌日から下痢がみとめられた。1日投与量を500mgに減量したところ下痢がとまり、投与を継続することが出来た。

尚、本剤投与前後に赤血球数、白血球数、Hb、GOT、GPT、BUN 値の臨床検査を行なった症例は11例であるが (Table 5)、このうち、症例25と症例36は基礎疾患に慢性肝炎があったため、トランスアミラーゼの上昇が認められた。しかし、その他の症例には本剤による異常な高値を示したものは1例もなかった。

Table 1 Report of cases treated with BAPC I

Case No.	Age & Sex	Diagnosis	Isolated organism	Dosage schedule			Combined surgery	Clinical course	Evaluation	Side effect
				g/day	Duration (day)	Total (g)				
1	67M	Furuncle of nucha		1.5	6	9	None	On the 3rd day, the core broke out spontaneously, and on the 5th day, all the signs and symptoms disappeared	Good	None
2	37M	Furuncle of right axilla	<i>Staph. epid.</i>	1.0	7	7	Incision	On the 3rd day, all the signs and symptoms disappeared	Excellent	None
3	41M	Furuncle of face	<i>Micrococcus</i>	1.0	7	7	Puncture	On the 3rd days signs and symptoms of infection disappeared	Excellent	None
4	32M	Carbuncle of hip	<i>Staph. aureus</i>	1.5	7	10.5	Incision	On the 5th day, signs and symptoms disappeared	Good	None
5	12M	Carbuncle of right elbow	<i>Staph. aureus</i>	0.75	4	3	Incision	On the 4th day, purulent discharge decreased	Good	None
6	17M	Carbuncle of right groin and scrotum		0.75	7	5.25	None	"	Good	None
7	20F	Felon of right thumb	<i>Staph. aureus</i>	1.0	5	5	Incision	On the 5th day, almost all the signs and symptoms of infection subsided	Good	None
8	22F	Paronychia of left thumb		1.0	5	5	Partial extraction of nail	On the 5th day, purulent discharge reduced	Good	None
9	61F	Felon of right thumb	<i>Staph. aureus</i>	1.5	7	10.5	Incision	On the 4th day, all the signs and symptoms subsided	Good	None
10	32F	Felon of left thumb	<i>Staph. aureus</i>	1.0	6	6	Incision	"	Good	None
11	67F	do	<i>Staph. aureus</i>	1.5	7	10.5	Incision	On the 5th day, all the signs and symptoms subsided	Good	None
12	26F	Cellulitis of back of left hand	<i>Staph. aureus</i>	1.0	10	10		On the 5th day, signs and symptoms disappeared, 7th day negative on culture	Good	None
13	26M	Cellulitis of left thigh	<i>Staph. aureus</i>	1.5	6	9	Incision	On the 4th day, signs and symptoms subsided, 5th day negative on culture	Good	None
14	46M	Cellulitis of left buccal region		0.75	10	7.5	Incision	By the 7th day, purulent discharge did not subside	Poor	None
15	25M	Cellulitis of left hip	<i>Staph. aureus</i>	0.75	7	5.25	Incision	Six days after the onset of infection, the patient consulted the clinic with severe complaints, and on the 3rd day of BAPC treatment pain, redness, swelling and purulent discharge subsided completely	Excellent	None
16	31F	Cellulitis of left thigh		0.75	6	4.5	Incision	On the 3rd day, the patient cured completely	Excellent	None
17	47F	Cellulitis of left dorsal foot	<i>Staph. aureus</i>	1.5	7	10.5		On the 7th day, signs and symptoms disappeared	Good	None
18	62M	Cellulitis of left wrist region	<i>E. coli</i>	1.0	7	7		On the 3rd, all the sign and symptoms disappeared	Excellent	None
19	51M	Infected atheroma cyst on the back	<i>Staph. aureus</i>	1.0	7	7	Incision	In 7 days of BAPC treatment, no relief of complaints was seen	Poor	None

Table 1 Report of cases treated with BAPC II

Case No.	Age & Sex	Diagnosis	Isolated organism	Dosage schedule			Combined surgery	Clinical course	Evaluation	Side effect
				g/day	Duration (day)	Total (g)				
20	31M	Infected atheroma cyst on the lumbar region		1.0	7	7	Incision	On the 5th day, cured completely	Good	None
21	56M	Infected atheroma cyst on left hip		0.75	3	2.25	Incision	On the 3rd day, pain and purulent discharge disappeared	Excellent	None
22	42F	Infected atheroma cyst on right scapular region	<i>Micrococcus</i>	1.0	9	9	Incision	On the 4th day, signs and symptoms of infections subsided	Good	None
23	64M	Infected atheroma cyst on the face	<i>Staph. aureus</i>	1.5	8	12	Incision	"	Good	None
24	31M	Infected atheroma cyst on the submaxillar region	<i>Staph. aureus</i>	1.5	8	12	Incision	By the 7th day, all the signs and symptoms disappeared	Fair	None
25	71M	Abscess of scrotum	<i>Proteus mirabilis</i>	1.0	10	10	Incision	On the 4th day, purulent discharge decreased	Good	None
26	30M	Perianal abscess		0.75	3	2.25		"	Good	None
27	50M	Abscess of scrotum	<i>Klebsiella Micrococcus</i>	1.0	8	8	Incision	On the 7th day, pain, redness and swelling disappeared, but purulent discharge continued	Fair	None
28	42F	Anal fistula, periproctal abscess	<i>Staph. epidermidis</i>	1.5	8	12	Incision	On the 6th day, purulent discharge reduced	Fair	None
29	34M	Periproctal abscess	<i>Klebsiella</i>	1.5	9	13.5	Incision	On 2nd day afebril and on 7th day purulent discharge subsided	Good	None
30	28M	Periproctal abscess	<i>E. coli</i>	1.5	7	10.5	Incision	Purulent discharge moderately decreased, but with positive culture	Poor	None
31	60F	Postoperative infection after the extirpation of atherom cyst		1.0	6	6		On the 4th day, redness and swelling disappeared	Good	None
32	45F	Postoperative infection after gastrectomy		1.0	5	5		"	Good	None
33	77M	Infected laceration of right palm	<i>Proteus mirabilis</i>	1.0	5	5		On the 3rd day, all the signs and symptoms subsided	Excellent	None
34	28F	Abscess of abdominal wall due to contaminated silk suture	<i>Micrococcus</i>	1.0	7	7		No improvement of infection, necessitating a reincision	Poor	None
35	16F	Recurrent post-operative infection after the operation of left inguinal hernia	<i>Staph. aureus</i> <i>Staph. epidermidis</i>	1.0 0.5	3 20	13.0		Purulent discharge decreased, but with positive culture	Poor	Diarrhea

Table 1 Report of cases treated with BAPC III

Case No.	Age & Sex	Diagnosis	Isolated organism	Dosage schedule			Combined surgery	Clinical course	Evaluation	Side effect
				g/day	Duration (day)	Total (g)				
36	35M	Infected fistula on left brachium	<i>Staph. aureus</i> <i>Proteus mirabilis</i>	1.0	15	15		BAPC therapy for 15 days could not control the contaminated granulation tissue	Poor	None
37	48M	Recurrent infected fistula of abdominal wall	G. N. R.	1.0	7	7	Incision	On 3rd day, all the signs and symptoms disappeared	Excellent	None
38	72F	Infected fistula of abdominal wall	G. N. R.	1.5	10	15		Fever continued with positive culture	Poor	None
39	46M	Osteomyelitis of right second proximal phalanx	<i>Staph. aureus</i>	1.0	11	11	Incision	On 7th day, purulent discharge reduced	Fair	None
40	63M	Osteomyelitis of left tibia and fibra	<i>Staph. aureus</i>	1.0	12	12		On 5th day, signs and symptoms of infection subsided	Good	None
41	72F	Acute cholecystitis		1.0	8	8		On 4th day, afebrile and on 8th day cholecystectomy performed with negative culture of bile	Good	None
42	34M	Peritonitis due to perforating gangrenous appendicitis	<i>E. coli</i>	1.5	11	16.5		On 7th day, purulent discharge reduced	Fair	None
43	41F	"	<i>E. coli</i>	1.5	12	18		On 6th day, fever subsided and purulent discharge reduced	Fair	None

Table 2 Criteria for evaluating effectiveness of an agent on infectious diseases

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 disappear within 7 days after onset of the treatment.
4. Poor	: Neither the symptoms and signs disappear nor their aggravation is observed after 7 days.

考 察

BAPC の血清中濃度は ABPC の経口投与後に比べて、すみやかにピーク値に達し、かつ ABPC の約 3 倍の高値を示すといわれている。また多くのグラム陽性菌およびグラム陰性菌などに対して幅広い抗菌スペクトル

をもち、なかでも、*E. coli* や *H. influenzae* に対する抗菌力は ABPC や AMPC と同程度にすぐれているという報告がある。われわれは今回外科的各種感染症 43 例に本剤を投与して、その治療効果を検討したが、これらの症例のなかに含まれる表在性感染症 40 例中、その 35 例 (87.5%) で明らかな臨床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。

本剤は ABPC のエステル化合物であるため、既述の如く消化管からの吸収が極めて良好であり、経口投与後 1 時間以内に血中濃度がピーク値に達し、かつ排泄も速やかである。一方、本剤の空腹時投与分では然らざる場合に比べて、血清中濃度は高いが、その持続時間はせいぜい 4 時間程度に限られている。それゆえ、われわれの症例では、本剤の経口投与方法を毎食後の 1 日 3 回、あるいは毎食後と就寝前の 1 日 4 回法に規定した結果、上述のような臨床治療効果をおさめることができた。今回のわれわれの症例は全般的に比較的軽症例が多かったため、この程度の投与量で上記の成績をおさめたものと

Table 3 Clinical effectiveness of BAPC on infections in the fields of surgery

Infectious disease	No. of cases	Excellent	Good	Fair	Poor	Side effect	Rate (%)
Furuncle-Caruncle	6	2	4				6/6
Felon	5		5				5/5
Cellulitis	7	3	3		1		6/7 (85.7)
Infected atheroma cyst	6	1	3	1	1		5/6 (83.3)
Periproctal abscess and Subcutaneous abscess of scrotum	6		3	2	1		5/6 (83.3)
Postoperative wound infection	5	1	2		2	1	3/5 (60.0)
Infected fistula	3	1			2		1/3 (33.3)
Osteomyelitis	2		1	1			2/2
Acute cholecystitis	1		1				1/1
Peritonitis due to perforating gangreous appendicitis	2			2			2/2
Total number of cases	43	8	22	6	7	1	36/43 (83.7)

Table 4 Comparison of bacterial response and clinical effectiveness

Organisms isolated	No. of cases	Bacterial response					Clinical effect				
		Disappeared	Decreased	Negative	Alternated	Unknown	Excellent	Good	Fair	Poor	Rate (%)
<i>Staph. aureus</i>	17	14	1	2			1	12	2	2	15/17 (88.2)
<i>Staph. epidermidis</i>	3	1		2			1		1	1	2/3 (66.7)
<i>Micrococcus</i>	4	2		1		1	2			2	2/4 (50.0)
<i>Proteus mirabilis</i>	3	2	1				1	1		1	2/3
<i>E. coli</i>	4	3		1			1		2	1	3/4 (75.0)
<i>Klebsiella</i>	2			2				1	1		2/2
G. N. R.	2	1		1				1		1	1/2 (50.0)
Total	35	23	2	9	0	1	6	15	6	8	27/35 (77.1)

Table 5 Laboratory findings in Bacampicillin administration

Case No.	Age & Sex	Diagnosis	Underlying	RBC ($\times 10^4$)		WBC ($\times 10^2$)		Hb		GOT		GPT		BUN	
				B	A	B	A	B	A	B	A	B	A	B	A
				12	26F	Cellulitis of back of left hand	Chronic hepatitis Cerebral hemiplegia	430	421	98	63	13.6	12.9	22	18
25	71M	Abscess of scrotum	330	314	112	84		10.0	9.8	66	60	52	48	6.0	8.0
29	34M	Periproctal abscess	Chronic hepatitis	443	429	102	81	13.9	13.1	19	21	17	20	—	—
32	45F	Postoperative infection after gastrectomy		381	322	53	52	11.8	10.5	12	16	18	21	12.5	8.5
36	35M	Infected fistula on left brachium		345	333	102	79	11.6	10.9	112	102	97	91	8.0	11.0
38	72F	Infected fistula of abdominal wall		321	343	44	51	11.9	12.1	30	29	26	23	—	—
39	46M	Osteomyelitis of right second proximal phalanx		402	411	106	53	15.0	14.5	22	12	9	6	7.0	9.0
40	63M	Osteomyelitis of left tibia and fibra		412	433	82	55	14.2	15.1	17	13	15	11	13.0	19.0
41	72F	Acute cholecystitis		378	—	170	108	13.4	—	32	28	24	20	—	—
42	34M	Peritonitis due to perforating appendicitis		398	453	128	52	15.9	14.0	15	—	26	—	16.2	16.3
43	41F	" "	401	378	99	67	14.3	13.4	28	27	26	25	—	—	

B: before A: after

考えられるが、症例によってはさらに投与量の増加も考慮されねばならない。なお、BAPCはester型であるためかなりの胃腸障害が予測されたが、われわれは原則として本剤を食後に投与したためか、このような副作用を経験していない。

結 論

BAPCを43例の外科的感染症例に投与し、著効+有効30例、やや有効6例、無効7例の結果をえ、重篤な副作用をみとめなかった。本剤は外科的感染症、特に表在性軟部組織の感染症に有効な新抗生物質として期待がもてる。

文 献

1) 第25回日本化学療法学会西日本支部総会、新薬シン

ポジウム Bacampicillin. 1977

- 2) BODIN, N.O.; B. EKSTRÖM, U. FORSGREN, L. P. JALAR, L. MAGNI, C. H. RAMSAY & B. SJÖBERG: Bacampicillin: a new orally well-absorbed derivative of ampicillin. *Antimicrob. Agents Chemother.* 8: 518-525, 1975
- 3) SWAHN, Å. Gastrointestinal absorption and metabolism of two ³⁵S-labelled ampicillin esters. *Europ. J. Clin. Pharmacol.* 9: 299-306, 1976
- 4) ROZENCWEIG, M., MAURICE STAQUET & JEAN KLASTERSKY: Antibacterial activity and pharmacokinetics of bacampicillin and ampicillin. *Clin. Pharmacol. Ther.* 19: 592-597, 1976

CLINICAL TRIAL OF BACAMPICILLIN IN THE FIELD OF SURGERY

AKINORI MASADA and FUKUO KITANO

Department of Surgery, Osaka Joto Chuo Hospital

KATSUJI SAKAI, MIKIO FUJIMOTO, SATORU HIRAO and TAKAMI UEDA

Second Department of Surgery, Osaka City University, Medical School Hospital

SUSUMU DOI

Department of Surgery, Osaka City Kita Hospital

AKIRA SAWADA

Department of Surgery, Osaka City Momoyama Hospital

TAKEYA SASAKI and SADAKUNI MAEDA

Department of Surgery, Fujiidera City Domyoji Hospital

NORIYUKI KAWABATA and YAEMON SHIRAHA

Department of Surgery, Ashihara Hospital

Bacampicillin, a new synthetic penicillin, was tried on 43 patients with infections in the field of surgery by means of oral administration.

The results obtained are summarized as follows: excellent and/or good responses were seen in 30 cases, fair in 6 cases, poor in 7 cases without any serious side effect. Conclusively, BAPC was thought to be a new antibiotic effective for acute infections of the soft tissues in the field of surgery.