Benzylpenicillin ineffective for open fractures

Prospective study of 60 cases

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In a prospective study of 60 open fractures treated with prophylactic antibiotics, 10 developed infection with 2/40 Grades 1 and 2 fractures and 8/20 Grade 3 fractures. Intravenous penicillin was ineffective against *Staphylococcus aureus* and *epidermidis*, the most usual organisms causing infection in open fractures, as 62 percent of the organisms cultured from the initial culture and 92 percent of those cultured during infection were resistant to penicillin. For the second generation cephalosporins, the respective figures were 21 and 30 percent.

Careful and immediate revision of the wound is the most important factor preventing infections in open fractures. The supplementary effect of antimicrobic treatment in the prevention of open fracture infections has varied (Table 1). Patzakis et al. (1974) compared antibiotic and placebo in the treatment of 310 open fractures. The infection rate was 2.3 percent in the antibiotic-treated group and 14 percent in the placebo group. Open fractures are contaminated and an effective antimicrobic with good penetration to the fracture hematoma should be administered to all of these patients (4).

We studied prospectively the effect of benzylpenicillin in the prevention of open fracture infections.

Patients and methods

Fifty-seven patients with a total of 60 open fractures treated at our hospital in 1984 participated in the present study. The mean age of the patients was 40 (8–87) years; 33 were males and 24 were females. The majority of the fractures were in the lower extremities (Table 2).

Open fractures were classified on the basis of the extent of soft-tissue damage (3). There were 20 each Grades 1, 2, and 3 fractures. Thirty-three patients had a single fracture, 13 patients had two or three fractures, and 11 patients had multiple fractures. Two patients had a concomitant vascular injury, and 3 had a pathologic fracture. A blood transfusion was given to 16 patients during the first 12 hours after the injury. Five patients had a medicated chronic heart failure, 1 patient was diabetic, and 7 patients were alcoholics.

Twenty-two open fractures were treated conservatively using plaster of Paris or traction. Internal fixation was used in 26 fractures and external fixation in 11 fractures. One fracture of the lower extremity was treated with primary amputation. Delays from accident to the initiation of antibiotic treatment and operation were recorded.

Table 1. Infection rates (percent) in open fractures

Reference	Antibiotic	Infection rate	n
5.	Cephalothin	2	84
	Penicillin - streptomycin	10	92
	Placebo	14	79
3.	Oxacillin - ampicillin	2	326
2.	Dicloxacillin	10	29
	Penicillin	3	31
	Placebo	20	30
6.	Cephamandole - aminoglycoside	5	109
1.	Clindamycin	6	34
	Cephazolin	7	42
7.	First-generation cephalosporins	13	238[a]
Present study	Penicillin	18	49

[a] Gunshot wounds excluded.

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Table 2. Observations in 60 open fractures

A	B	C	D	E	F	G	H	I
1	74	F	1	3	+	1	3	1
2	32	M	1	1	+	1	1	1
3	15	M	1	2	+	1	2	2
4	30	F	1	3	+	1	3	2
5	72	M	1	3	+	2	3	2
6	15	M	1	3	+	1	1	1
7	27	M	1	3	+	1	1	1
8	32	M	1	3	+	1	2	1
9	80	F	1	3	+	1	2	2
10	38	M	1	3	+	1	2	2
11	18	F	1	3	-	1	2	0
12	26	M	1	3	+	1	2	0
13	56	M	1	1	+	1	1	0
14	14	M	1	1	+	1	1	0
15	13	F	1	2	+	1	1	0
16	33	M	2	1	+	1	1	0
17	48	M	1	1	+	2	1	0
18	29	M	2	2	+	1	1	0
19	9	M	2	1	+	1	1	0
20	19	M	1	2	+	1	3	0
21	71	F	2	1	+	1	3	0
22	19	M	1	1	+	2	3	0
23	36	F	1	1	+	2	3	0
24	87	F	2	3	+	1	2	0
25	17	M	1	3	+	1	4	0
26	71	F	1	3	+	1	1	0
27	58	M	2	1	+	1	1	0
28a	29	M	1	3	+	2	3	0
28b	29	M	2	2	-	2	1	0
29	22	M	1	2	+	1	3	0
30	33	M	2	2	+	1	3	0
31	60	F	1	1	+	1	3	0
32	32	F	2	2	+	1	3	0
33	53	F	1	1	+	1	3	0
34	45	F	2	1	+	1	3	0
35	53	F	2	2	+	1	2	0
36	55	M	1	3	+	1	2	0
37	37	F	1	3	-	2	2	0
38	37	F	1	2	-	2	3	0
39	35	M	1	2	-	1	3	0
40	17	M	1	1	-	1	3	0
41	17	M	1	2	-	1	3	0
42	42	M	1	1	-	1	3	0
43	69	F	1	2	+	1	3	0
44	25	M	2	2	-	1	3	0
45	58	F	1	2	-	1	3	0
46	26	M	2	2	-	1	3	0
47	63	F	1	3	-	2	3	0
48	71	F	1	3	-	2	2	0
49a	27	M	1	1	-	1	1	0
49b	27	M	1	3	-	1	1	0
50	18	F	1	2	-	1	1	0
51a	72	F	2	1	-	1	1	0
51b	72	F	2	2	-	1	1	0
52	8	F	2	1	-	1	1	0
53	62	F	1	1	-	1	1	0
54	46	M	1	1	-	1	1	0
55	54	M	1	2	-	1	3	0
56	29	M	1	2	-	1	1	0
57	25	M	2	3	-	2	1	0

A case
B age
C sex
D injured extremity: 1 lower, 2 upper
E grade
F primary culture
G antibiotic: 1 benzylpenicillin, 2 cephalosporins
H fracture fixation
1 closed
2 external
3 internal
4 amputation
I infection: 0 no infection, 1 superficial, 2 deep

An initial wound swab was taken before the administration of antibiotics. Intravenous benzylpenicillin, 4-million IU four times daily, was given routinely to 47 patients, excluding 10 patients allergic to penicillin; they received intravenous cephalosporins, 750–1,500 mg 3-4 times daily. Patients treated with cephalosporins had more often Grade 3 fractures (6/10) than those treated with benzylpenicillin (14/47). The antibiotic treatment was initiated before wound revision and fracture treatment, and it was continued for 3 days.

The criteria for a superficial infection were local swelling, redness, tenderness, pus formation, and bacterial growth in the wound. A deep infection was recorded when the patient had a positive radiograph and possibly a delayed union or a nonunion of the fracture in addition to the signs of superficial infection.

The chi-square test, Student's *t*-test, and regression analysis were used. *P*-values less than 0.05 were considered significant.

Results

Delays from accident to the initiation of antimicrobic treatment and operation showed no correlation to open-fracture infection. Of the initial wound cultures, 60 percent were positive. Totally, 64 percent of the cultured organisms showed resistance to benzylpenicillin and 21 percent to second-generation cephalosporins. A single organism was found in 27 percent and several organisms in 28 percent of the initial wound cultures.

Infection developed in 10 open fractures (four pin-tract infections excluded) within 12 (2–30) days. *Staphylococcus aureus* and *S. epidermidis* were the most commonly detected organisms during infection (4 and 6 cases, respectively). *Enterococcus* was cultured from two infections and *Pseudomonas* from one infection. The same organisms were cultured at the initial stage and during infection in 5 cases. Twelve organisms out of 13 showed resistance to benzylpenicillin and 3 to second-generation cephalosporins. Infection occurred in 9/49 of the benzylpenicillin-treated fractures and in 1/11 of the cephalosporin-treated fractures.

A positive initial wound culture was associated with a higher risk of fracture infection ($P < 0.05$). Infection developed in 8/20 of Grade 3 fractures compared with 2/40 Grades 1 and 2 fractures ($P < 0.001$). Infection developed in 3/5 of the internally fixed, in 3/9 of the externally fixed, and in 2/5 of the

conservatively treated Grade 3 fractures. Both patients with a concomitant vascular injury developed an infection. Patients with one fracture had an infection less often than the rest ($P < 0.005$). Multiple fractures, a compensated heart failure, a pathologic fracture, diabetes, and alcoholism did not seem to increase the risk of infection.

The average hospital stay was 73 (30–180) days for patients with an open-fracture infection. Five patients developed a deep osteomyelitis, and the infection persisted at least 6 months in 3 patients.

Discussion

In the present study, *Staphylococcus aureus* and *S. epidermidis* were the most frequently cultured organisms from the wound at the initial stage, as well as during infection. *Staphylococcus aureus* was resistant to penicillin and sensitive to cephalosporins. *Staphylococcus epidermidis* was frequently resistant to penicillin (62 percent), but sensitive to cephalosporins. Other infection-causing organisms (*Enterococcus* and *Pseudomonas*) were highly resistant to penicillin and cephalosporins. Antibiotics used in the early treatment of open fractures have a slight effect on these organisms. In a study by Roth et al. (1986), preoperative antibiotic treatment did not yield better results when compared with peroperative treatment in open fractures. In their series, *Pseudomonas* and *Enterococcus* were the most often cultured pathogens during infection, and these pathogens were considered to have been acquired in the hospital.

In the present study a positive wound culture at the initial stage indicated an increased risk of infection. In half of the infections the same organisms were cultured at the initial stage and during infection. However, because no tests to confirm the phage type were performed, the origin of the pathogen was not clear. Like in our study, Patzakis et al. (1974) found a positive wound culture in the early stage in two thirds of the open fractures. In their series the organisms causing infections were present in the first culture in 41 percent of the cases.

In the present study, penicillin was found to be ineffective in the treatment of open fractures. The fear of multiresistant hospital pathogens has led to great cautiousness in the use of broad-spectrum prophylactic antibiotics in open fractures. However, the incidence of open fractures is so low that the use of broad-spectrum antibiotics in the early treatment of open fractures would not substantially increase the development of such multiresistant pathogens. *Staphylococcus aureus* and *S. epidermidis*, as well as streptococci and *Clostridium*, are pathogens that can and should be controlled by early antibiotic treatment of open fractures.

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