

Penicillin G versus cefuroxime for prophylaxis in lower limb amputation

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Out of 457 patients amputated below or above the knee, we randomized 228 to receive penicillin G and 229 cefuroxime as prophylaxis against infection. We also stratified the patients into two groups: Group A (313 patients) who did not receive antibiotic treatment within 48 hours prior to the operation and Group B (88 patients) who did. There were 56 dropouts according to protocol regulations. The patients were evaluated for efficacy on the 21st postoperative day. In Group A, 20 of 158 (13 per cent) penicillin G-treated and 27 of 155 (17 per cent) cefuroxime-treated had wound sepsis; 5 (3 per cent) penicillin G-treated and 4 (3 per cent) cefuroxime-treated patients had been reamputated by Day 21 ($P > 0.05$). We concluded that prophylactic penicillin G prevents infection as effectively as cefuroxime after lower limb amputation.

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The value of prophylactic antibiotics in lower limb amputation has been demonstrated (Møller and Krebs 1985, Sonne-Holm et al. 1985): cefoxitin and methicillin were both better than placebo in reducing the rate of wound sepsis and reamputation. However, penicillin G has previously been recommended to reduce gas gangrene after lower limb amputation (Taylor 1960, Parker 1969).

We investigated whether prophylaxis with new broad-spectrum cephalosporin is preferable to penicillin G.

Patients and methods

From August 1, 1984 to April 1, 1986, 457 patients admitted for a lower limb amputation in 19 centers were randomized to prophylaxis with cefuroxime or penicillin G after informed consent.

Six of the centers enrolled less than 15 patients each, while the remaining 13 centers enrolled from 15 to 62 patients. Excluded were patients with known allergy to cephalosporins or penicillin G or amputation through the knee. Reamputations were not included as new cases.

At the start of anesthesia and 4 and 12 hours later, 288 patients received 3 g penicillin G and 229 patients 1.5 g cefuroxime; both drugs were given intravenously. Because many patients were already treated with antibiotics owing to infected gangrene or general sepsis, they were stratified into two groups: Group A (313 patients) received no antibiotics 48 h prior to the amputation and Group B (88 patients) had already received antibiotics within that time. The surgical technique and postoperative treatment followed the routines of the various orthopedic departments (Table 1). The sutures were removed after 14 to 21 days. The wounds were evaluated 3 weeks postoperatively. In case of wound sepsis, swabs were taken for aerobic and anaerobic cultures.

The patients in each randomized group were comparable regarding sex, age, occurrence of diabetes mellitus, skin perfusion measurement, operative technique, and postoperative bandage (Table 1). Fifty-six patients in Group A, 27 treated with penicillin G and 29 with cefuroxime, could not be evaluated because of allergic manifestations, treatment with other antibiotics within 48 hours postoperatively, or withdrawn consent (Table 2). Seventeen penicillin G- and 10 cefuroxime-treated patients died within 3 weeks without septic or other wound complications. These patients were excluded from the statistical analysis.

For statistical calculations, the chi-square and the Fischer exact tests were used.

Results

In Group A the frequency of primary healing, dry necrosis, wound sepsis, and reamputation was similar independent of antibiotic treatment (Table 3). The results in Group B were similar to those in Group A (Table 4).

In none of the subgroups in Group A or B were the differences obtained between the two antibiotics significant. In about half of the patients in Group A, no measurement of skin perfusion preceded the amputation; 22 of these had wound sepsis and 6 were reamputated before Day 21.

There was no difference between the effect of penicillin G and cefuroxime in patients who had had preoperative skin perfusion measurements and no difference between patients with or with-

Table 1. Descriptive parameters of 457 amputated patients

	Penicillin G	Cefuroxime
Number	228	229
Sex		
Female	128	129
Male	100	100
Age		
Mean	75	74
Range	44-104	40-94
Amputation		
Below the knee	151	144
Above the knee	77	85
Diabetes mellitus	88	78
Skin perfusion measurement		
Below the knee (10 cm)		
<30 mmHg	12	14
30-40 mmHg	18	23
>40 mmHg	68	70
Not done	130	122
Above the knee (10 cm)		
<30 mmHg	1	3
30-40 mmHg	2	1
>40 mmHg	11	7
Not done	214	219
Surgical technique		
Below the knee		
Long posterior flap	62	62
Sagittal	58	55
Fish-mouth	23	22
Other	8	5
Above the knee		
Simple	26	26
Myoplastic	51	59
Drainage	222	227
Bandage		
Closed plaster cast	15	15
Padded plaster splint	71	61
Soft bandage	138	147
Other	4	6
Dropouts	27	29

Table 2. Randomization and stratification of 457 amputated patients

	Group A		Group B	
	Penicillin G	Cefuroxime	Penicillin G	Cefuroxime
Below the knee	107	98	28	30
Above the knee	51	57	15	15
Total	158	155	43	45
Dropouts	27	29		

out a preceding skin perfusion measurement ($P > 0.05$). No difference was found when comparing the results from patients treated with a soft or a hard bandage.

S. aureus was isolated from 5 penicillin

Table 3. Efficacy evaluation groups

Score	Below the knee		Above the knee	
	Penicillin G	Cefuroxime	Penicillin G	Cefuroxime
Healed	61 (61)	47 (51)	32 (78)	37 (70)
Dry necrosis	20 (20)	19 (21)	2 (5)	6 (11)
Wound sepsis	15 (15)	20 (22)	5 (12)	7 (13)
Reamputated at same level	0	0	^a	0
Reamputated at higher level	4 (4)	3 (3)	0	1 (2)
Dead from wound complication	0	3 (3)	2 (5)	2 (4)
Dead without wound complication ^b	7	6	10	4
Total	107	98	51	57

Numbers in brackets are rate in percent.

^a One patient was reamputated at the same level but died with wound complication.

^b Excluded from the efficacy evaluation.

G-treated patients and from 4 cefuroxime-treated patients in Group A. In Group B the corresponding figures were 0 and 1. One penicillin G- and 1 cefuroxime-treated patient, both more than 85 years old, died of gas gangrene: *C. perfringens* was isolated from one of the patients.

Discussion

Sonne-Holme et al. (1985) and Møller and Krebs (1985) using cefoxitin and methicillin, respectively, clearly demonstrated that prophylactic antibiotics should be given after lower limb amputation. In our investigation, cefuroxime was as effective as penicillin G, and the incidence of wound sepsis was comparable to Sonne-Holm et al. (1985).

The difference in vitro between cefuroxime and penicillin G is the activity against penicillinase-

Table 4. Efficacy evaluation Group B

Score	Below the knee		Above the knee	
	Penicillin G	Cefuroxime	Penicillin G	Cefuroxime
Healed	19 (70)	18 (62)	10 (77)	7 (54)
Dry necrosis	3 (11)	4 (14)	0	3 (23)
Wound sepsis	4 (15)	3 (10)	3 (23)	3 (23)
Reamputated at same level	0	1	0	0
Reamputated at higher level	1 (4)	3 (10)	0	0
Dead from wound complication	0	0	0	0
Dead without wound complication ^b	1	1	2	2
Total	28	30	15	15

Numbers in brackets are rate in percent.

^b Excluded from the efficacy evaluation.

producing staphylococci (Garrod et al. 1981). The high penicillin G dosage used was chosen to achieve very high concentrations, thus preventing *S. aureus* to adhere.

In our study also the dropouts were evaluated. It is noteworthy that the results for these patients and the patients in Group B were the same as in Group A. When looking at the 457 patients as one group and comparing penicillin G with cefuroxime, no difference could be found.

Two of our patients died of gas gangrene. This and the relatively high number of wound complications and reamputations demonstrate that the present surgical technique, use of disinfectants and prophylactic antibiotics can reduce, but not abolish serious complications. The only real difference between the two antibiotic regimens was the price: cefuroxime was almost five times as expensive as penicillin G.

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