A comparison of short- and long-term intravenous antibiotic therapy in the postoperative management of adult osteomyelitis

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The current standard recommendation for antibiotic therapy in the management of chronic osteomyelitis is intravenous treatment for six weeks. We have compared this regime with short-term intravenous therapy followed by oral dosage.

A total of 93 patients, with chronic osteomyelitis, underwent single-stage, aggressive surgical debridement and appropriate soft-tissue coverage. Culture-specific intravenous antibiotics were given for five to seven days, followed by oral therapy for six weeks. During surgery, the scar, including the sinus track, was excised *en bloc*. We used a high-speed, saline-cooled burr to remove necrotic bone, and osseous laser Doppler flowmetry to ensure that the remaining bone was viable. Infected nonunions (Cierny stage-IV osteomyelitis) were stabilised by internal fixation. In 38 patients management of dead space required antibiotic-impregnated polymethylmethacrylate beads, which were exchanged for an autogenous bone graft at six weeks. Free-tissue transfer often facilitated soft-tissue coverage. These 93 patients were compared with 22 consecutive patients treated previously who had the same surgical management, but received culture-specific intravenous antibiotics for six weeks.

Of the 93 patients, 80 healed without further intervention. Of the 31 Cierny-IV lesions, 27 healed without another operation, and four fractures required additional bone grafts. No more wound drainage was needed. Treatment was successful in 91% of patients, regardless of the organism involved. There was no difference in outcome in terms of these

variables when the series were compared. We conclude that the long-term administration of intravenous antibiotics is not necessary to achieve a high rate of clinical resolution of wound drainage for adult patients with chronic osteomyelitis.

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Many regimes of treatment have been designed to prevent, suppress, arrest and ameliorate osteomyelitis.¹⁻⁸ Treatment principally involving long-term antibiotics has been disappointing, with rates of recurrence of approximately 30%.⁹⁻¹¹ The management of osteomyelitis relies on a multidisciplinary approach, combining debridement, soft-tissue cover and antimicrobial therapy to give the patient the best chance of cure.^{3,12-14} However, treatment has not been standardised.

The general recommendation for the early stages of osteomyelitis has been parenteral antibiotics.¹⁵⁻¹⁸ Therapy for four to six weeks has been reported to achieve an acceptable rate of cure.¹⁵⁻²⁰ The cost of intravenous antibiotics at home for six weeks can range from US\$3500 to US\$10 000.²¹ The rate of serious complications from the use of intravenous catheters ranges from 10% to 30%.^{6,22} Total costs for oral antibiotics are lower, with equal effectiveness for the treatment of chronic osteomyelitis.²³⁻²⁶ Once extensive devascularisation and necrosis of bone occur, antibiotic therapy alone is ineffective.^{27,28} The use of laser Doppler flowmetry accurately reflects the perfusion status of bone and is a useful adjunct to surgery.^{7,8,28}

We have compared the clinical outcome of the treatment of a series of patients with osteomyelitis by single-stage, aggressive surgical debridement utilising osseous laser Doppler flowmetry and appropriate soft-tissue coverage followed by intravenous antibiotics for five to seven days and oral therapy for six weeks, with that of a historical series treated with the same surgical protocol and intravenous antibiotics for six weeks.

Patients and Methods

We reviewed retrospectively the medical records, surgical reports and radiographs of 93 consecutive patients treated at Harborview Medical Centre in Seattle from February

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Table I. A comparison of the 93 patients in the study group who received short-term intravenous antibiotics followed by oral antibiotics for six weeks, with a series of 22 historical control patients who received intravenous antibiotics for six weeks

	Study group	Control group	p value
Gender (%)			
Male	76	86	
Female	24	14	
Mean age in years ($\pm$ sd)	45 $\pm$ 15	40 $\pm$ 16	
Bone involvement (%)			
Tibia	60	59	
Femur	20	27	
Other	16	14	
Bone location (%)			
Proximal	34	23	
Diaphyseal	34	55	
Distal	32	22	
Cierny stage (%)			
I	6	0	
II	14	0	
III	46	36	
IV	34	64	
Delayed bone graft			
Autograft (%)	37	64	>0.05
Antibiotic-impregnated beads			
Yes (%)	41	18	>0.05
Wound coverage (%)			
None	43	41	
Local	22	32	
Free tissue	33	27	
Follow-up (mth)	31	18	

1989 to January 1995. This group of patients was compared with 22 historical controls treated from 1986 to 1988 by the same orthopaedic surgeon (MFS) in collaboration with microvascular surgeons (DH, NV). A comparison of the two groups is shown in Table I.

In the study group there were 71 men with a mean age of 43 years (18 to 77) and 22 women with a mean age of 48 years (31 to 70). The anatomical site of infection was identified (Table II). The cause of the infection was judged to be haematogenous in seven, after breakdown of a surgical wound in 15, and post-traumatic in the remainder. The injuries included 43 open fractures, 25 closed fractures, and three thermal injuries. Treatment consisted of open reduction and internal fixation in 57 patients, closed reduction with a cast in six, and external fixation in eight.

At the time of presentation, 80 patients had been treated with intravenous antibiotics, 35 by previous removal of metal, 22 by previous soft-tissue procedures, and one by a vascularised bone graft. These patients averaged four (0 to 16) surgical debridements before inclusion in our group. Two patients had had no previous treatment.

Between the diagnosis of osteomyelitis and inclusion in our study, 37 patients had constant and four intermittent wound drainage. The remainder had dry wounds but had intermittent drainage previously for a mean of 48 months (0 to 708). The mean time from the original diagnosis to infection was 84 months (0 to 616). Significant comorbid-

ities included smoking in 60 patients (65%), psychiatric disorders in 16 (17%), obesity in 11 (12%), peripheral vascular disease in 10 (11%), and diabetes mellitus in 2 (2%). Osteomyelitis was divided into four stages as described by Cierny et al;¹ medullary (type I) in 6 patients, superficial (type II) in 13, localised (type III) in 43, and diffuse (type IV) in 31 (Table I).

Laboratory assessment included a complete blood count with an absolute neutrophil count, measurement of the ESR and nutritional screening. Recent biplanar radiographs were used for radiological evaluation. Radio-isotope bone scans, CT and MRI were not part of the assessment although most patients presented to us with these studies already completed.

The wound was approached surgically by sharply excising the scar, including the sinus track, *en bloc* down to the infected bone. A cutaneous specimen was examined for atypical squamous cells. Granulation tissue was eliminated with a rongeur, and the membrane curetted off the bed of bone. Aggressive debridement utilising a high-speed, saline-cooled burr removed necrotic bone. Osseous laser Doppler flowmetry signals in excess of 100 mV were used to ensure that all remaining bone was viable; the normal level for cortical bone is 100 mV.^{7,8,28} For patients with Cierny stage-IV osteomyelitis and nonunion, the bone was stabilised after debridement by internal fixation. All wounds were closed primarily. Dead space was managed by the insertion of polymethylmethacrylate beads containing tobramycin, with vancomycin added when *Staphylococcus* infection was considered a possibility, which were replaced by autogenous bone graft after six weeks. Soft-tissue coverage was obtained by primary wound closure using local tissue when possible and rotational or free-tissue transfer when necessary (Table I). In the 93 patients, antibiotic selection was influenced by previous culture

Table II. Anatomical site of osteomyelitis for the 93 patients in the study group

Bone and site	Number of patients
Femur	
Proximal	4
Diaphyseal	7
Distal	6
Tibia	
Proximal	24
Diaphyseal	15
Distal	22
Fibula	
Proximal	0
Diaphyseal	0
Distal	2
Humerus	
Proximal	1
Diaphyseal	1
Distal	0
Pelvis	4
Other	7

results. When this information was not available the patient was started on intravenous gentamicin and vancomycin. Parenteral antibiotics for a median of five days were narrowed to organism-specific therapy when necessary. Patients were discharged from hospital with a six-week supply of oral antibiotics. The oral antibiotic of choice was trimethoprim (160 mg), sulphamethoxazole (800 mg) (double strength, twice daily) with ciprofloxacin, 750 mg twice daily, as the alternative. The historical series of 22 patients was treated with intravenous antibiotics for six weeks based on the result of tests for culture and sensitivity.

Patients were contacted by telephone to determine the presence of drainage, walking ability and the use of walking aids.

Statistical analysis. Categorical variables were compared between the two groups using chi-squared tests of association; Fisher's exact test was used when appropriate. The Wilcoxon signed-rank test was used to compare continuous variables.

Results

Deep cultures were obtained at the time of the surgical debridement (Table III). A total of 31 patients had multiple organisms with 17 having mixed aerobic and anaerobic. The most common organism, *Staphylococcus aureus*, was found in 54 patients, including 22 of the 31 with multiple-organism infections. Other organisms included *Pseudomonas* species in 21 patients, *Staphylococcus epidermidis* in ten (one of whom had Cierny stage-IV osteomyelitis), *Enterobacter* species in six, *Proteus* species in two and other Gram-negative species in 13. No anaerobes were isolated.

Debridement often resulted in considerable tissue defects. Antibiotic-impregnated beads were used to fill bone defects in 38 patients and, with rare exception, were replaced at six weeks by autogenous bone graft. Local tissue transfer in 20 patients, including 12 medial gastrocnemius, one soleus, one lateral arm, one gracilis, and five fasciocutaneous flaps provided soft-tissue coverage. A free-tissue transfer was required in 33 patients, including 17 latissimus dorsi, 12 gracilis and four other flaps (Table I).

Five patients have subsequently died. In one this can be related to the initial osteomyelitis and subsequent treatment. The patient was a 75-year-old man who had sus-

tained a closed fracture of his femur 56 years before treatment for osteomyelitis. He had experienced polymicrobial drainage for 30 years and had severe emphysema necessitating chronic oxygen therapy. He died from post-operative pulmonary complications.

There were three subsequent amputations, one for squamous-cell carcinoma in a sinus track and two for persistent drainage. The latter two patients were considered failures of treatment, and are included in the follow-up series of 87 patients. The mean follow-up for this group was 31 months (0 to 62). A total of 80 fractures healed without further complication. Four delayed unions healed with additional bone grafts. At the latest follow-up, only one patient had nonunion. After the initial closure, 79 (91%) patients did not experience further wound drainage. Four patients used canes, one a walker, and one a brace, but 78 walked without assistance. One patient, who was not able to walk before treatment, was not able to do so afterwards.

Discussion

Achieving eradication of drainage for adults with chronic osteomyelitis is difficult, involves complex protocols of treatment, and may be expensive. Our regime of aggressive debridement and appropriate soft-tissue coverage, with intravenous antibiotics for five to seven days and oral antibiotics for six weeks, proved to be successful in most cases. The magnitude of the surgery can be underscored by our one perioperative death. The savings in cost from intravenous antibiotic administration for a limited period warrant further study.

There are three basic mechanisms by which osteomyelitis may occur. Haematogenous osteomyelitis affects the long bones of children¹⁵⁻¹⁸ but is rare in adults except for vertebral involvement.²⁹ Such patients often have infection by a single organism as was seen in 14 patients with haematogenous osteomyelitis in our study.

Osteomyelitis from vascular insufficiency is often the sequel of diabetes mellitus.¹⁷ Contiguous osteomyelitis most often follows injury to limbs.¹⁶ In contrast to haematogenous osteomyelitis, these last two often result in polymicrobial infections, frequently *Staphylococcus aureus* mixed with other pathogens. We did not routinely culture the sinus tracks of draining wounds since the bone pathology is often not represented at the surface wound.³⁰ The work of Cierny^{1,6,22} and others has demonstrated that the outcome of osteomyelitis is dependent upon the degree of bony involvement and the nature of the host.^{9,31} Our study confirms this, and emphasises the importance of identifying the extent of avascular bone and excising with a limited blood supply. Antibiotics cannot reach devitalised tissue.²⁸

Initial injury damages the vascular supply of bone and soft tissue. The rate of infection correlates directly with the type of fracture, which is based on the extent of soft-tissue injury.^{5,32,33} As infection extends through the soft tissue, the vascular supply is further compromised. If both medul-

Table III. Microbial profile of deep cultures obtained at the time of surgical debridement for the 93 patients in the study group and the 22 patients in the control group

	Study group	Control group
<i>Escherichia coli</i>	0	1
<i>Morganella morganii</i>	0	2
Polymicrobial	31	7
<i>Pseudomonas</i>	5	2
<i>Serratia marcescens</i>	1	1
<i>Staphylococcus aureus</i>	18	4
<i>Staphylococcus epidermidis</i>	7	5
Other	5	0
Unknown	26	0

lary and periosteal blood supplies are affected, sequestra may be formed.³⁴ Despite an intense host response, surgery, and antibiotic therapy, bacteria may be difficult to eradicate secondary to the ischaemic and necrotic tissue. Non-viable bone is the best substrate for chronic and acute infections.²⁸ Laser Doppler flowmetry may facilitate an accurate assessment of the microvascular status of bone, thereby identifying it for removal.^{7,8}

To reduce the potential for infection further, soft-tissue cover was provided when the defect could not be closed primarily. Free-tissue transfers were used³⁵⁻³⁸ in both this study and for the historical series. In studies on bacterial inoculation after free-tissue transfer,³⁵ it was found that a musculocutaneous flap can increase the resistance to bacterial infection. It can be argued that vascularised tissue allows the delivery of antibiotics to an area of established osteomyelitis.³⁵ The success of the flap leads to the successful treatment of the infection with adherence of soft tissue to the viable bone surface.²⁸

More than 60% of our patients were smokers. The effect of nicotine on bone microperfusion is the suspected mechanism. It has been shown that while preoperative and postoperative smoking markedly increased the incidence of necrosis of flaps,³⁷ preoperative cessation of smoking decreased it. In an analysis of the efficacy of free-tissue transfer in the two-stage treatment of osteomyelitis³⁸ patients were treated with antibiotics for seven to ten days after radical debridement followed by an additional three to seven days at the time of free-tissue transfer. Thirty out of 37 (79%) grafts survived and there were five amputations. We used one-stage debridement and free-tissue transfer in this study as well as in the historical series and had only one flap failure.

Short-term intravenous antibiotic therapy was effective and independent of the organism. Although there are some dissimilarities between the current series and our historical control group, they appear to be comparable (Table I). We suggest that it would not be possible to assess the two protocols of short- and long-term intravenous therapy in a randomised, controlled trial because of the multiple variables of bone, region, host status, aetiology, Cierny stage, and organism, and the difficulty of sufficiency of material in a single centre because of the incidence of adult chronic osteomyelitis. Based on the results of our study, we believe that it is safe to use short-term intravenous therapy followed by oral therapy for six weeks for the management of adult chronic osteomyelitis after adequate surgery.

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