Treatment of 112 bone and joint infections with teicoplanin*

Traitement de 122 infections ostéo-articulaires avec la Teicoplanine

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Abstract: Teicoplanin was used in three hospitals over 6 years in 112 cases of bone or joint infection and the results were reviewed retrospectively. Teicoplanin was used at a dose of 400 mg/day, after a 3-day loading regimen, in combination with other agents, usually netilmicin at the beginning of the treatment. Most infections were chronic (mean duration = 20.9 months) and had failed previous antibiotic or surgical treatment. Gram-positive organisms were isolated in 120/137 identified strains (64 methicillin-resistant Staphylococcus aureus or coagulase negative Staphylococci) and all were susceptible to teicoplanin except one (intermediate for NCCLS norms). Median of follow-up was 17.3 months. The final outcome was clinical cure in 89/98 evaluable cases (91%). There were one improvement, four failures and four recurrences. Adverse events occurred in 11 patients (0%) but did not require any change in treatment. Despite the limitations of a retrospective study, teicoplanin appeared to be effective, well tolerated and easy to use with only one daily injection.

Key words: Teicoplanin — Gram-positive organisms — Bone infection — Joint infection

Teicoplanin is a glycopeptide antibiotic active against most Gram-positive bacteria, including methicillin-resistant Staphylococci. The minimum inhibitory concentration (MIC90) of teicoplanin is 0.2-3.1 mg/l against 90% of Staphylococcus aureus strains, irrespective of methicillin resistance [1]. There is a wider range of teicoplanin MIC90 (0.2-12.5 mg/l) against coagulase-negative staphylococci, particularly with some isolates of Staphylococcus haemolyticus with decreased susceptibility to teicoplanin.

Teicoplanin has a good diffusion in bone, with a single dose of 6 mg/kg i.v. leading to a mean concentration [2] of 46.3 (± 11) mcg/ml in the serum, of 10.8 (± 6.8) mcg/g in cancellous bone and 6.1 (± 1.7) mcg/g in cortical bone after 30 minutes. Twenty four hours later, the authors found a mean concentration of 3.3 (± 1.7) mcg/ml in the serum, 7.1 (± 5.4) mcg/g in cancellous bone and 4 (± 2.5) mcg/g in cortical bone.

Teicoplanin can be given i.m. or i.v. as a bolus or a short infusion with a low risk of red man syndrome, it has a long half-life, allowing once-daily dosage and, after an initial check, routine monitoring of serum concentrations is not required. These characteristics make teicoplanin particularly suitable for the prolonged treatment of serious chronic bone and joint infections at home as well as in hospital.

Although there are no controlled studies of its use in bone and joint infections, teicoplanin has been found to be effective in a number of open trials [4, 5]. A dose of 6 mg/kg/day appears adequate for the treatment of osteomyelitis, but 12 mg/kg/day has been advocated for septic arthritis [6]. The present study reviewed the efficacy and safety of teicoplanin, 6 mg/kg/day, in combination with other antibiotics in the treatment of 112 episodes of bone or joint infection.

Method

A retrospective review was undertaken of 110 patient files corresponding to 112 episodes of bone or joint infection treated with teicoplanin between 1988 and June 1994. Patients were treated in three different hospitals: 50 in Institut Calot (Berck), 38 in Hopital de la Croix Rousse (Lyon) and 34 in Hopital Rene Sabran (Giens). The following items were recorded: demographic details, type of infection, presence of prosthetic material, previous treatment, causative patho-
organisms were isolated in 120 cases, and all were susceptible to teicoplanin except one (Table 2). The most common pathogen was S. Aureus (72 cases) and most isolates were resistant to methicillin (42 cases); the MICs of teicoplanin for 13 methicillin-resistant strains were 0.5-8 mg/l, while for eight methicillin-sensitive strains the MICs of teicoplanin were 0.06-4 mg/l. Coagulase-negative staphylococci were isolated in 33 infections and 22 were methicillin resistant. The MICs for three methicillin-resistant strains of coagulase negative Staphylococci were 2 mg/l, 8 mg/l and 16 mg/l (the only strain defined as Intermediate). In 26 patients, more than one organism was isolated, usually a Staphylococcus plus an aerobic Gram-negative (Klebsiella, Acinetobacter or Pseudomonas...). Gram-negative bacteria were not isolated in pure culture from any patient.

The standard dosage of teicoplanin was used in 95 out of the 112 episodes. Fourteen patients did not receive a loading regimen and in three the dosage was unknown.

The duration of treatment varied from 6 to 707 days with a median of 28 days and a mean of 51 days. All patients received concomitant antibiotics. Sixteen antibiotics were recorded, usually aminosides (45), fluoroquinolones (44), fusidic acid (29), fosfomycin (20), pyostacin (11), rifampicin (9) and others (18). One concomitant antibiotic was given in 50 cases, two (concomitant or consecutive) antibiotics were given in 48 cases, and ten patients received three (concomitant or consecutive) antibiotics in addition to teicoplanin. Further antibiotics (usually administered orally) were given after the course of teicoplanin in 93 patients, monotherapy in 49 and combination in 44. Fluoroquinolones (41: 26 ofloxacin, 8 pefloxacin, 7 ciprofloxacin), pristinamycin (33), fucidic acid (22) and rifampicin (18) were common choices.

One hundred patients had surgery (Table 1). In particular all foreign materials (prosthetic or osteosynthetic) was removed except two total hip and one total knee replacements, and all chronic osteitis and osteomyelitis had been operated.

The median serum C-reactive protein (normal ≤2 mg/l) was 47 mg/l (4-398 mg/l) before and 8 mg/litre (3-253 mg/l) after treatment.

Follow-up lasted from 1 week (a non operated bursitis) to 66 months with a median of 13 months and a mean of 17.3 months. The patients were considered as a success if there were none of the signs of infection (clinical or bacterial) at the last consultation. 14 cases (12 patients) were not evaluable because they were lost (Tables 1 and 3).