Cefamandole and Isoxazolyl Penicillins in Antibiotic Prophylaxis of Patients Undergoing Total Hip or Knee-joint Arthroplasty

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Summary. In a prospective comparative clinical efficacy and safety study, 58 patients undergoing total hip or knee arthroplasty were randomly allocated to two groups; one received 29 cefamandole intravenously before operation and then 1 g every 6 h parenterally for 3 days and the other received 29 cloxacillin i.v. every 8 h for 1 day and 29 dicloxacillin perorally every 8 h for 2 days. Concentrations of cefamandole and cloxacillin were measured in the serum of all patients and in the synovial fluid of 28 patients. The serum C-reactive protein (CRP) level was measured in 16 randomly allocated patients preoperatively and daily for 8 days. In serum the concentrations of cefamandole and cloxacillin were high. The great variation in cloxacillin concentration can be due in part to its strong affinity for blood proteins. Cefamandole entered the synovial fluid of the knee joint at high concentrations in 5-15 min; similar concentrations of cloxacillin were measured after 16-30 min. Thus, cefamandole seems to be more recommendable as antibiotic prophylaxis in total hip and knee replacements. The CRP level decreased to below 60 mg/l in all 16 patients on the 6th postoperative day.

Parenteral antibiotic prophylaxis or bone cement with antibiotic is used in total hip or knee replacements. Due to this prophylaxis, early infections in hip arthroplasties have decreased from 5.8% to 0.5% – 2% [8].

The beginning time and length of antibiotic prophylaxis in arthroplasty vary greatly. Schurmann et al. [7] recommended starting the prophylaxis in the operating room and giving antibiotics for 3 days. Even 1-day prophylaxis has been considered sufficient [3], but 2-weeks antibiotic prophylaxis has also been used [6].

The purpose of this study was to compare cefamandole and isoxazolyl penicillins as agents of antibi-otic prophylaxis in hip and knee joint arthroplasties. Special attention was also paid to changes in serum C-reactive protein (CRP) levels.

Patients and Methods

Fifty-eight consecutive patients undergoing total hip or knee replacement for osteoarthrosis in our department between 1983 and 1984 were included in this study. Revision arthroplasties were excluded. The mean age of the patients was 67.4 years, range 54–79 years. Forty-four of them were women and 14 men. The follow-up time was at least 2 years.

The patients were randomly allocated to two groups. There were no significant differences in age, sex, or weight among the groups. Each patient was given a 2-g dose of antibiotic intravenously over a 10-min period after anesthesia had been established and just before the operation began. After that, one group received 1 g cefamandole every 6 h parenterally for 3 days and the other received 2 g cloxacillin every 8 h intravenously for 1 day and then 1 g dicloxacillin perorally for 2 days. In patients undergoing total knee replacement (nine in each group), the tourniquet was inflated approximately 15 min after the antibiotic was given.

Blood samples were taken to obtain a serum level at the time the joint capsule was opened in all patients. Samples of synovial fluid were obtained in 28 patients by means of needle aspiration prior to the opening of the capsule. The concentration of antibiotics in serum and in synovial fluid was determined. The time between the end of the antibiotic injection and taking the sample was registered.

In addition to the clinical examination, preoperative chest radiographs and electrocardiograms were taken. Transfusions compensated for blood loss during the operation (average
Suction drainage was maintained for 24 h after surgery. The following laboratory examinations were done before operation and on the third and seventh postoperative days: hemoglobin, hematocrit, erythrocyte sedimentation rate (ESR), serum creatinine, electrolytes (sodium, potassium), protein, alkaline phosphatase, transaminase enzymes (S-ASAT, S-ALAT), and uric acid. Serum CRP was determined turbidometrically preoperatively and then daily during the first 8 postoperative days in 16 randomly allocated patients. Axillary temperature was also measured daily for 8 days.

**Results**

During anesthesia, one patient developed allergic urticaria due to the cloxacillin injection. One patient in the isoxazolyl group had a superficial wound infection which healed without any action. Four patients in each group had axillary temperatures of 38°C or more on at least 1 day during the first postoperative week. The recovery of these patients was uneventful. Preoperative ESR was approximately 17 mm. A postoperative maximum mean ESR value was 61 mm, and there was only a slight decrease during the first 8 days. One patient in each group had a minor transient increased level of S-ASAT and S-ALAT. There were no signs of leukocytosis or increases in creatinine concentrations above the normal values.

Six patients had symptomless cystitis, which was found in preoperatively taken cultured specimens. The pathogen was sensitive to cefamandole in all cases, but in the cloxacillin-dicloxacillin group a different treatment had to be used.

The concentration of cefamandole in synovial fluid was two thirds of that in serum after 5 min. The variation in the concentration of cloxacillin was great, and after 15-30 min the concentration in the synovial fluid of the knee joint was less than half of that in the serum (Tables 1-3).

The preoperative CRP level was normal (< 10 mg/l) in all patients but rose rapidly after surgery. Maximal values (50–132 mg/l) were reached within 24–48 h but the CRP level decreased to below 60 mg/l in all 16 patients on the sixth postoperative day (Fig. 1).

There was no deep infection or loosening of the endoprosthesis during the 2-year follow-up.

**Discussion**

Dicloxacillin is better absorbed than cloxacillin, but it has a very high degree of protein binding in blood.