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ORIGINAL ARTICLE

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# Effects of air tourniquet on the antibiotics concentration, in bone marrow, injected just before the start of operation

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**Abstract** Infection is one of the most serious complications after artificial arthroplasty. In order to establish the effective prevention for after operative infection, we measured the serum and bone marrow blood cefmetazole (CMZ) concentration time dependently (1 g CMZ, one shot). Furthermore, we studied the effect of air tourniquet on CMZ transmit into bone marrow blood. Thirteen knees with total knee arthroplasty (TKA) were included in the study. As a control group, 11 hips with total hip arthroplasty (THA) were also included. In TKA, air tourniquet was used during operation in all cases. Just before the start of the operation, 1 g CMZ was injected intravenously (one shot). Subsequently we sampled peripheral blood and bone marrow blood time dependently. Cefmetazole concentration was measured with HPLC. In the THA group, serum and bone marrow blood CMZ concentration showed almost the same time-dependent change. On the other hand, in the TKA group we could not detect CMZ in bone marrow blood in cases where CMZ was injected within 8 min before starting use of an air tourniquet. If CMZ was injected more than 10 min before starting use of the air tourniquet, CMZ concentration in bone marrow blood was much lower than minimum inhibitory concentration (MIC) for *Staphylococcus aureus*; but after releasing the air tourniquet, CMZ concentration in bone marrow blood was higher than MIC for *S. aureus*. These data suggested that our injection method is effective for prevention of infection both during and just after operation in the THA but in the TKA, CMZ should be injected more than 10 min before starting to use the air tourniquet.

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## Introduction

Recently, for treatment of osteoarthritis (OA) and/or rheumatoid arthritis (RA), many artificial arthroplasties have been performed, and good clinical results regarding artificial arthroplasty have been reported. However, postoperative infection is one of the most serious complications following artificial arthroplasty, which might result in loss of joint function, amputation, or sepsis.[1] The infection rate after total hip arthroplasty (THA) and total knee arthroplasty (TKA) was reported to be 0.8% and 2.1%, respectively, in Japan in 1986,[2] with the most common clinical isolates being *Staphylococcus aureus* and *Staphylococcus epidermidis*.[2] It is very important for prevention of intra- and postoperative infection to use an effective spectrum of antibiotics against these organisms.

Cefmetazole (CMZ; Cefmetazon) is the second-generation cefamycin, and has a very broad spectrum from Gram-positive cocci to Gram-negative bacilli.[3–6] We reported that CMZ could transmit into bone marrow blood.[7]

In orthopedic surgery on the extremities, an air tourniquet is used frequently. Using the air tourniquet can affect the antibiotics as they are transmitted into bone marrow. In this study, in order clarify the effects of an air tourniquet on antibiotics concentration in bone marrow blood, we measured the concentrations of CMZ injected just before the start of operation for THA and TKA in both peripheral blood and bone marrow blood, time dependently.

## Materials and methods

Twelve patients (two men and ten women, mean age 68.5 years), 13 knees with TKA for osteoarthritis (OA) (in five), and rheumatoid arthritis (RA) (in seven) were included in the study. As a control group, ten patients (all

**Table 1.** Cases in this study

| | Disease | Mean age (range) | Sex |
|---|---|---|---|
| TKA group | OA 5 cases, 5 joints<br>RA 7 cases, 8 joints | 68.5 years (51–82 years) | Male 2 cases<br>Female 10 cases |
| THA group | OA 10 cases, 11 joints<br>RA 0 case, 0 joint | 65.3 years (48–77 years) | Male 0 case<br>Female 11 cases |

TKA, total knee arthroplasty; THA, total hip arthroplasty; OA, osteoarthritis; RA, rheumatoid arthritis

women, mean age 65.4 years old), 11 hips with THA for OA (Table 1) were included. All patients were informed that the data from the blood and bone marrow blood samples from the case would be submitted for publication, and gave their consent.

In TKA, the air tourniquet was used at 400 mmHg during operation in all cases. Just before the start of operation, 1 g CMZ was dissolved in 20 ml saline, and one shot was injected intravenously. Following this we sampled peripheral blood from the arterial line and bone marrow blood from the femur in the operative field, time dependently. We took serum samples from the blood by centrifuge, and stored these at –20°C until measurement. Bone marrow blood samples were stored without centrifugation. Bone marrow blood was homogenized with buffer. The CMZ concentration was measured in both serum and bone marrow blood using high-performance liquid chromatography in Institute of Science and Technology (minimal concentration 0.5 μg/ml or 0.5 μg/g). All patients in this study were negative for intracutaneous test of CMZ before injection.

We divided the patients into two groups: the TKA group in which an air tourniquet was used during operation, and the THA group operated on without the tourniquet. The data from the two groups were compared. Furthermore, in the TKA group we studied the timing of injection for prevention of infection prior to use of the air tourniquet.

## Results

In both TKA and THA groups, CMZ serum concentration decreased time dependently (Fig. 1). In the THA group, both serum and bone marrow blood CMZ concentration showed almost the same time-dependent changes (Figs. 2 and 3), and the ratio of bone marrow blood concentration, and serum CMZ concentration was almost constant (58%–71%). On the other hand, in the TKA group we could not detect CMZ in those cases where CMZ was injected within 8 min before starting to use the air tourniquet. Furthermore, there was no time-dependent change even in the cases of CMZ injection 8 min or more before starting to use the air tourniquet, and those concentrations were much lower than those in the THA group. In the TKA group, CMZ concentrations in bone marrow blood after relieving the air tourniquet were 61%–134% of those in serum, those data being equal to or higher than CMZ concentrations in bone marrow blood in the THA group (Table 2).

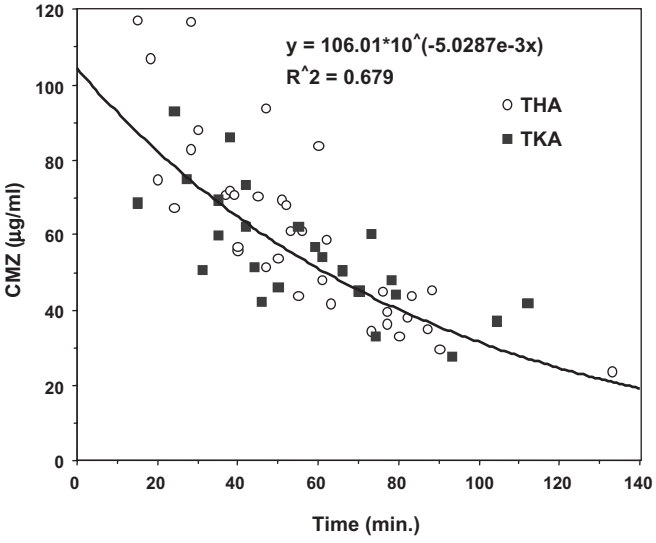


**Fig. 1.** Time-dependent changes of serum cefmetazole (*CMZ*) concentration, 1 g one-shot injected in both total hip arthroplasty (*THA*) and total knee arthroplasty (*TKA*) groups

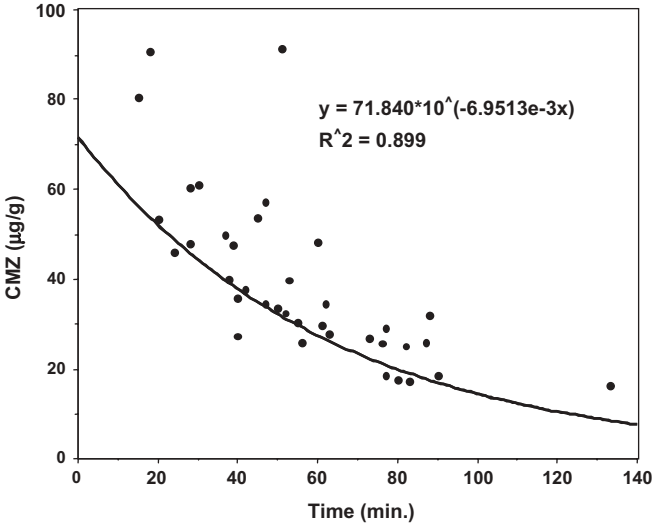


**Fig. 2.** Time-dependent changes of bone marrow blood CMZ concentration, 1 g one-shot injected in the THA group

The minimal inhibitory concentration (MIC) of CMZ against *S. aureus* is reported as 3.13 μg/ml.[3] In our data, the serum CMZ concentration stayed at a higher level than MIC against *S. aureus* for 234 min in the TKA group and for 174 min in the THA group (Fig. 1). In the TKA group,

**Table 2.** Bone marrow blood CMZ concentration in total knee arthroplasty group

| Case | CMZ injection timing before or after starting to use air tourniquet (min) | 0–30 min (μg/g) | 31–45 min (μg/g) | 46–60 min (μg/g) | 61–75 min (μg/g) | 76–90 min (μg/g) | 91–120 min (μg/g) | 121–150 min (μg/g) |
|---|---|---|---|---|---|---|---|---|
| 1 | After 6 | ND | 1.1 | ND | ND | | | |
| 2 | After 2 | ND | ND | 2.4 | | | | |
| 3 | After 1 | ND | ND | ND | | | | |
| 4 | Before 6 | ND | | 0.6 | ND | ND | | |
| 5 | Before 8 | 1.2 | 0.9 | | 2.7 | | | |
| 6 | Before 11 | 0.9 | 5.8 | | 1.3 | 16.2 | | |
| 7 | Before 12 | | 24.1 | | | 1.1 | 6.7 | |
| 8 | Before 12 | 27.6 | | ND | ND | | 45.7 | |
| 9 | Before 14 | | 44.3 | ND | ND | | ND | |
| 10 | Before 14 | | 1.0 | | 1.0 | | | |
| 11 | Before 16 | | | ND | ND | | 0.5 | 29.9 |
| 12 | Before 19 | | 40.3 | | ND | | 24.6 | 20.3 |
| 13 | Before 22 | | | | 0.8 | ND | ND | 23.3 |

Underlined data show CMZ concentration after releasing tourniquet
CMZ, cefmetazole; ND, not detected

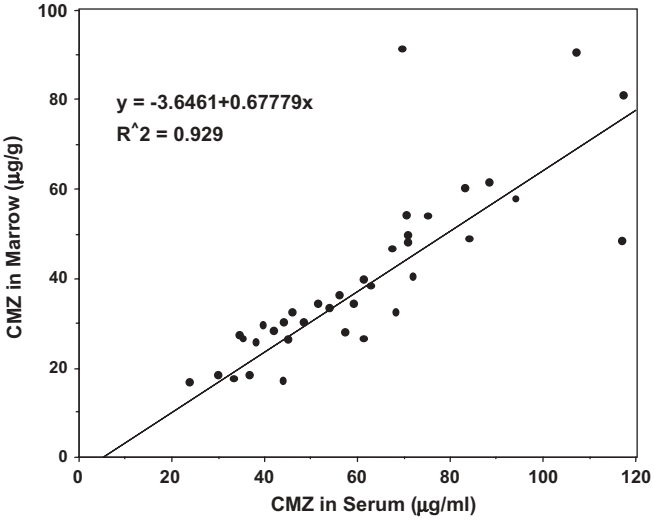


**Fig. 3.** Relationship of serum and bone marrow CMZ concentration, 1 g one-shot injected in the THA group

after relieving the air tourniquet the CMZ concentration in bone marrow blood (93–136 min after injection) showed a higher level than MIC against *S. aureus*.

## Discussion

As THA and TKA surgeries involve insertion into the bone and joints of substantial artificial material, in cases where infection after operation occurs it is very difficult to cure. Therefore it is very important that operative wound infection be prevented.[1]

In 1986 the infection rates after THA and TKA were reported to be 0.8%, and 2.1%, respectively.[2] In Murray's reported data on his 808 THA cases over 4 years from 1968, the infection rate after operation was 0.77% in the cases that used antibiotics during operation but was 3.96% in the cases where no antibiotics were used.[8] Based on these data, in bone and joint surgery involving insertion of large implants into the body, especially for immunocompromised hosts, we should use the minimum amount of adequate antibiotics for prevention of postoperative infection.[9] Matsushita and Aoki reported that prophylactic antibiotics should be injected before the start of the operation, and on skin incision the serum antibiotic concentration should be high enough to prevent infection.[10]

The MIC of CMZ against *S. aureus* is reported to be 3.13 μg/ml.[3] In our data the serum CMZ concentration stayed higher than 3.13 μg/ml for 234 min in the TKA group and for 174 min in the THA group. These times are long enough to complete the operation of either THA or TKA. In the THA group, both serum and bone marrow blood CMZ concentration showed almost the same time-dependent changes, and the ratio of bone marrow blood CMZ concentration to serum concentration was almost constant (58%–71%). These data suggest that bone marrow blood CMZ concentration might directly depend on serum concentration. On the other hand, in the TKA group using the air tourniquet our data clearly showed that we should inject CMZ 8 min or more before starting to use the air tourniquet (Table 2). However, if CMZ was injected less than 10 min before starting to use the air tourniquet, CMZ concentration in bone marrow blood did not show at the MIC level for *S. aureus* (Table 2), whereas if we injected CMZ more than 10 min before starting to use the air tourniquet, we might be able to keep CMZ concentration higher than the MIC level for *S. aureus*. On the point of infection prevention during the operation, we should inject CMZ more than 10 min before starting to use air tourniquet in the operation of TKA. Furthermore, we need a new method for injection of antibiotics, for example, intravenous local antibiotics injection, immediately prior to operation.[11]

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