ORIGINAL ARTICLE

# Antibiotic prophylaxis in hip surgery: A comparision of two vs. three doses of cefuroxime

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## Abstract

**Objective:** To compare the efficacy of two-dose regime with a three-dose regime of cefuroxime in the prevention of post-operative wound infection in hip surgery patients and to determine the most effective regime of antibiotic prophylaxis for such patients.

**Methods:** The prospective, comparative, multi-centre cohort study was conducted from January 1998 to June 1998 at Dundee Royal Infirmary and attached district hospitals (Stirling Royal Infirmary and Falkirk Royal Infirmary). It comprised patients who had hip surgery i.e. fracture fixation, hemiarthroplasty or total hip replacement. Patients were assigned to two groups. Group A patients received cefuroxime 750mg at induction of anaesthesia and 750mg at the end of the procedure, while Group B patients received 1.5gm of cefuroxime at the induction of anaesthesia, followed by 750mg 8 and 16 hours after the operation. Patients were assessed post-operatively daily according to the ASEPSIS wound scoring system during the hospital stay.

**Results:** There were 280 patients in the study, with 140(50%) in each of the two groups. In Group A 60(43%) patients required fracture fixation, the rate of wound infection was 2(3.3%), 40(28.5%) required hemiarthroplasty and the rate of wound infection was 1(2.5%) and 40(28.5%) required total hip replacement and the rate of wound infection was zero. In Group B, the corresponding numbers were 1/60 (1.6%), 1/40 (2.5%) and zero. No evidence of minor, moderate or severe wound infection was observed in 272(97%) patients regardless of the group. The most frequent pathogens were Staphylococcus aureus in 3(1%) patients and Staphylococcus epidermidis in 2(0.7%).

**Conclusion:** There was no significant difference in the prevalence of wound infection between the patients who had received two or three doses of cefuroxime.

**Keywords:** Antibiotic prophylaxis, Cefuroxime, ASEPSIS, Hip surgery, THR, Staphylococcus aureus, Staphylococcus epidermidis, UTI, Wound infection. (JPMA 65: S-136 (Suppl. 3); 2015)

## Introduction

In 1970's and early 1980's, antibiotic prophylaxis was shown to be more effective than placebo, in the prevention of post-operative wound infection in patients who had hip surgery.[1-3] However despite considerable clinical research, there is still no consensus regarding the duration of antibiotic prophylaxis for hip surgery.[4,5] Fractures of the proximal part of the femur in adults are treated operatively either with internal fixation or by hemiathroplasty. The reported rate of wound infection associated with internal fixation has ranged from 5-16%.[6-8] and with hemiarthroplasty or total hip replacement (THR) the infection rates range from 1-2%.[2,3,9,17]

Pre-operative antibiotic prophylaxis given for two days or more has been shown to decrease the frequency of infection, but it may promote the growth of resistant bacterial strains.[18] Cephalosporins have been recommended for antibiotic prophylaxis because of their broad spectrum of activity and low toxicity.[19] Cefuroxime has been approved for use as single preoperative dose and may be followed up by 24 hours of prophylaxis after the operation.[15,17,19]

The current study was planned to compare the efficacy of a two-dose and three dose regimes of cefuroxime in the prevention of post-operative wound infection in patients, who had hip surgery and to determine the most effective regime of antibiotic prophylaxis for these patients.

## Patients and Methods

The prospective, comparative, multi-centre cohort study was conducted from January 1998 to June 1998 at Dundee Royal Infirmary hospital and attached district hospitals (Stirling Royal Infirmary and Falkirk Royal Infirmary hospital). The patients had open reduction and internal fixation (ORIF) of proximal femoral fracture with dynamic hip screw (DHS), cannulated screws or pugh nail plate, hemiarthroplasty or total hip replacement (THR) as

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elective primary or revision surgery.

Patients who were excluded had received a systemic or topical antibiotic up to 7 days before operation, had a history of allergy to antibiotics or needed antibiotic prophylaxis for other reasons (i.e. prosthetic heart valve) or who died within one week of operation.

Power calculations revealed that in order to show the significant difference with 80% power the study required about 3000 patients.

After approval from the institutional review committee and informed consent from all patients, the study sample was divided into two groups according to the doses of cefuroxime. Group A patients belonging to the Dundee Royal Infirmary received 750mg cefuroxime intravenously (IV) at induction of anaesthesia, followed by 750mg IV at the end of the procedure. Group B patients belonging to the two district hospitals received cefuroxime 1.5gm IV at induction of anaesthesia and 750mg IV 8 and 16 hours post-operatively.

Pre-operative variables included age, American Society of Anesthesiologists (ASA) classification,[20] pre-operative indwelling urinary catheter, type of surgery (fracture fixation, hemiarthroplasty or THR).

Operative variables included duration of operation, number of drains or use of any local antibiotics i.e. bone cement impregnated with gentamicin.

Post-operative variables included disturbance of wound healing or infection according to the ASEPSIS scoring system,[21] number of post-operative blood transfusions, urinary catheter and urinary tract infections and pulmonary infection such as pneumonia.

The infections were graded as local or systemic according to specific criteria. Local infections were assessed daily according to ASEPSIS scoring system, which is a daily point scale system for wound infection and the points are later added together to produce the final score.[21-22]

Systemic infection was defined by the presence of urinary tract infection or pulmonary infection. A positive mid-stream or catheter specimen urine culture was indicative of urinary tract infection. A positive sputum culture was diagnostic of pulmonary infection.

All hospitals involved in the study had a laminar flow theatre ventilation system and central supply department for sterilisation of instruments.

Data was entered in the excel spread sheet. Mean ± standard deviation was calculated for age, duration of admission, duration of operation, number of post-operative blood transfusions and number of patients having wound problems. Frequency and percentages were calculated for the rest. T-Test was applied on quantitative data, with $p < 0.05$ being considered significant.

## Results

Out of 280 patients in the study, 120(43%) had ORIF of proximal femoral fracture with DHS, cannulated screws or pugh nail plate; 80(28.5%) had hemiarthroplasty and 80(28.5%) had THR as elective primary or revision surgery.

The two groups had 140 (50%) each. The demographic

**Table-1:** Pre-operative data.

| Characteristics | Group A | | | Group B | | |
|---|---|---|---|---|---|---|
| | Fx Fix | Hemi | THR | Fx Fix | Hemi | THR |
| **Age (years)** | | | | | | |
| Mean | 82 | 79 | 71 | 78 | 82 | 67 |
| Range | 55-100 | 50-98 | 52-86 | 46-96 | 59-98 | 45-86 |
| Male Patients | 8 | 5 | 20 | 12 | 4 | 7 |
| Female Patients | 52 | 35 | 20 | 48 | 36 | 33 |
| **Duration from admission to operation (No. of Days)** | | | | | | |
| Mean | 1.2 | 1.1 | 1 | 0.86 | 1 | 1.5 |
| Range | 0-5 | 1-4 | 1-2 | 0-2 | 0-3 | 1-11 |
| **Duration from admission to discharge (No. of Days)** | | | | | | |
| Mean | 17.3 | 18.9 | 13.2 | 15.1 | 17.3 | 19 |
| Range | 1-4 | 1-85 | 6-32 | 4-58 | 6-28 | 13-92 |
| **ASA Class** | | | | | | |
| Mean | 2.4 | 2.3 | 1.5 | 2.2 | 2.2 | 2.1 |
| Range | 1-4 | 2-3 | 1-2 | 1-3 | 2-3 | 1-3 |
| No of patients who had pre-op urinary catheters | 10 | 5 | 4 | 16 | 15 | 8 |

Fx fix: Fracture Fixation, ASA: American Society of Anaesthesia, Hemi: Hemiarthoplasty, THR: Total hip replacement.

**Table-2:** Data on operations and risk factors.

| Character | Group A | | | Group B | | |
|---|---|---|---|---|---|---|
| | Fx Fix | Hemi | THR | Fx Fix | Hemi | THR |
| Duration of Operation (Mins) | 82.2 | 80.5 | 124.3 | 95.8 | 80.3 | 164.5 |
| Mean(Average) | (40-180) | (45-165) | (75-210) | (40-310) | (45-135) | (105-240) |
| **Number of Drains** | | | | | | |
| Mean | 0.08 | 0.35 | 0.7 | 1.03 | 1.1 | 1.9 |
| Range | 0-1 | 0-1 | 0-2 | 0-2 | 1-2 | 1-3 |
| Number of patients with indwelling urinary catheter post-operatively | 19 | 19 | 15 | 30 | 23 | 22 |
| **Number of post-op blood transfusions** | | | | | | |
| Mean | 0.9 | 0.6 | 1.4 | 1.03 | 0.9 | 3.1 |
| Range | 0-7 | 0-3 | 1-4 | 1-13 | 0-4 | 0-11 |
| **Number of patients who had wound problems** | | | | | | |
| Disturbance of wound healing | 1 | 1 | 1 | 2 | 2 | 1 |
| **Minor wound infection** | | | | | | |
| Moderate wound infection | 2 (3.3%) | 1 (2.5%) | 0 | 1 (1.6%) | 1 (2.5%) | 0 |
| **Severe wound infection** | | | | | | |
| Number of patients who had systemic infection | | | | | | |
| Urinary | 8 | 2 | 1 | 4 | 1 | 2 |
| Pulmonary | 2 | | | 1 | | |

Fx fix: Fracture Fixation, Hemi: Hemiarthoplasty, THR: Total hip replacement.

**Table-3:** Relationship of urinary tract infection to indwelling urinary catheter.

| Characteristics | Group A | | | Group B | | |
|---|---|---|---|---|---|---|
| | Fx Fix | Hemi | THR | Fx Fix | Hemi | THR |
| **No. of patients who had urinary catheters** | | | | | | |
| Pre-operative | 10 | 5 | 4 | 16 | 15 | 8 |
| Post-operative | 19 | 19 | 15 | 30 | 23 | 22 |
| **No. of patients who had urinary tract infection** | | | | | | |
| With catheter | 6 | 1 | 2 | 3 | 1 | 2 |
| Without catheter | 2 | 0 | 0 | 1 | 0 | 0 |
| Total | 8 | 2 | 1 | 4 | 1 | 2 |

Fx fix: Fracture Fixation, Hemi: Hemiarthoplasty, THR: Total hip replacement.

characteristics of the two groups were compared in terms of age, gender, duration of pre-operative hospitalisation, duration of hospitalisation from admission to discharge, ASA class, primary diagnosis, operative procedure, duration of operation and presence of risk factors (Tables-1 and 2).

In Group A, 60(43%) patients required fracture fixation and the rate of wound infection was 2(3.3%); 40(28.5%) required hemiarthroplasty and the rate of wound infection was 1(2.5%) and 40(28.5%) required THR and the rate of wound infection was zero. In Group B, the corresponding numbers were 1/60 (1.6%), 1/40 (2.5%) and zero. No evidence of minor, moderate or severe wound infection was observed in 272(97%) patients regardless of the group.

During the post- operative hospital stay, there were 8(2.8%) patients who had disturbance of wound healing and 5(1.7%) had moderate wound infection according to the ASEPSIS wound scoring system. Overall rate of infection was 5/200 (2.5%) in fracture fixation and hemiarthroplasty. There was no infection in those who had THR.

There was no statistical difference in the prevalence of wound infection between the groups. The 8(3%) patients who had some disturbance of wound healing (ASEPSIS score 11-20) all responded to local wound care without antibiotics. No patient with disturbance of wound healing progressed to wound infection. The 5(2%) patients who had moderate wound infection were managed with systemic antibiotics and 2(0.7%) were debrided.

The most frequent pathogens were S. aureus in 3(1%) patients and S. epidermidis in 2(0.7%) patients. All the

organisms were sensitive to cefuroxime. There were no significant differences in patient characteristics (p>0.05), but it was noted that of the 8 patients who had disturbance of wound healing, 4(50%) had duration of operation more than 3 hours, 2(25%) had more than 10 post-operative blood transfusions and all (100%) had post-operative urinary catheter.

The 5 patients who had wound infection and had post-operative urinary catheters 3(60%) had urinary infection with positive catheter specimen urine culture. Urinary tract infection developed in 11 (7%) patients in Group A and 7 (5%) in Group B. Of the 18 patients who had urinary tract infection, 15 (83%) had postoperative indwelling urinary catheter and 3(17%) patients did not have indwelling urinary catheter (Table-3). With respect to pulmonary infection, pneumonia developed in 2(1.4%) patients in Group A and 1 (0.7%) patients in Group B.

## Discussion

Experimental studies that have been conducted since 1961 show that antibiotics can reduce that rate of incisional infections when these are administered shortly before the incision is made on the skin.[18,23,25] The antibiotics must be present in the blood in sufficient concentrations at the time of bacterial contamination which has been shown to occur even during so-called clean operations.[10,18] These observations influenced the design of recent clinical studies, with patients being given antibiotics at the induction of anaesthesia. Antibiotics were found to be clinically effective in preventing infection, but when the operation has lasted for more than four hours, a second course of antibiotics is necessary.[26,27] A study on the efficacy of antibiotics in the prevention of infection during abdominal operation showed that antibiotic coverage beyond 24 hours did not provide additional protection.[28]

Shorter antibiotic prophylaxis regimens have been recommended[3,13] for hip surgery, but these recommendations have been made on the basis of personal experience or have been extrapolated from data on other operative procedures rather than on the basis of published results of prospective well-designed clinical studies. The results of the present study indicated that there is no significant difference in the prevalence of wound infection between the patients who had either received 2 or 3 doses of cefuroxime.

This study compared the same drug cefuroxime administered on different dosage schedules and was designed to detect differences in the overall rate of wound infection. The difference in the rate of infection was 1% in patients with fracture of the proximal femur treated by internal fixation or had hemiarthroplasty and 0% in patients with THR. To determine if this difference was statistically significant we would require more patients in each treatment group. Power calculations reveal that if we have to show the significant difference with 80% power, we require about 1500 patients in each group and in these hospitals it will take 10 years to complete the research.[29] It is difficult to prove the efficacy of one antibiotic regime over another when the rate of infection is so low and the numbers are so small.

The rate of wound infection was 2.5% for the fracture surgery in both subgroups of patients who had fracture internally fixed or replaced with hemiarthroplasty and 0% for the THR.

The rates are similar to those previously reported for fracture surgery.[3,9,11,13,16,17,30,34]

The rate of disturbance of wound healing for the patients who had fracture proximal part of femur, either fixed or replaced was 3% and for those who had THR was 2.5% in both groups.

The selection of antibiotic for the prophylaxis is empirical and should be based on the results of controlled clinical studies and on local antimicrobial susceptibility pattern. In the present study staphylococcus aureus and staphylococcus epidermidis were the isolated pathogens.[35,36] These results confirm that the antibiotic selected for operative prophylaxis should be active against staphylococcus.[15,17,26]

Antibiotics are often administered for three days post-operatively, despite reports that administration of antibiotics for more than 24 hours provide no additional benefit.[5,11,13,17,28,33,34] Our study confirms that short courses of prophylactic antibiotic regimes are safe and cost-effective. The cost of the regimen in Group A was cheaper than regimen in Group B. The two-dose regimen also differs in several other important aspects. First of all, the total dose of cefuroxime is half that of the 3-dose regimen. Secondly, both of the doses of two-dose regimen were administered in theatre during the period of maximum risk where as two doses in the 3-dose regimen were administered positively in the ward and therefore may have no additional benefit.

Some studies have suggested that the duration of operation can alter the rate of infection.[10] In our study the average duration of operation varied for different procedures. However the results revealed that increase in operation time was associated with an increase in the disturbance of wound healing. So, a second dose of prophylactic antibiotic is recommended if the operation

time exceeds more than three to four hours.[24,26]

Bone surfaces continue to seep after orthopaedic procedures and therefore drainage tubes are often used. This presents a potential source of bacterial contamination. In the present study post-operative drainage did not appear to influence the prevalence of wound infection (Table-2). Our study results are similar to those reported earlier.[15]

It is also shown in some series[10,12,35] that homologous blood transfusions increase the risk of acute post-operative infective complications. In our study it was also noticed that patients who were transfused 10 units had some disturbance of wound healing.

A study[37] found that the microorganisms that grew on culture of material from the wound were not the same as those that grew on culture specimens of the urine. Our results showed that 3 (60%) patients who had wound infection also had urinary tract infection but the microorganisms that grew on the culture material from the wounds were not the same as those grown on culture from the specimen of urine. However, we noted that most of the patients with urinary tract infection (83%) had an indwelling urinary catheter and this supports the comments in literature,[38] that 90% incidence of noscomial urinary tract infections are due to catheterisation. Our results support a study[11] which concluded that incidence of urinary tract infections is more dependent on the indwelling urinary catheter than the number of days of antibiotic prophylaxis.

## Conclusion

There were no significant differences in the prevalence of wound infection between patients who received either 2-dose or 3-dose regimen of cefuroxime for prophylaxis of infection in hip surgery. As such, short-term antibiotic prophylaxis for hip surgery is recommended.

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