

Cloxacillin as an Antibiotic Lock Solution for Prevention of Catheter-Associated Infection

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Keywords. catheter-related infections, bacteremia, hemodialysis, cloxacillin

Introduction. Catheter-related infection is associated with increased all-cause mortality and morbidity in hemodialysis patients. This study aimed to evaluate an antimicrobial lock solution (cloxacillin and heparin) in temporary noncuffed double-lumen catheters for long-term intermittent hemodialysis as a method of preventing catheter-related infection.

Materials and Methods. Patients on hemodialysis with noncuffed temporary double lumen catheter were randomly divided into 2 groups. Fifty patients received a solution containing cloxacillin, 100 mg/mL, plus heparin, 1000 IU/mL as a 2.5-mL solution instilled in each of catheter lumens after dialysis session. Another 50 patients received only heparin. They were allowed to dwell until the next session of dialysis.

Results. One catheter-related bacteremia was observed in the antibiotic group whereas catheter-related bacteremia was observed in 8 of those who received heparin only. The rate of catheter-related bacteremia episodes were 0.5 per 1000 catheter-days in the antibiotic group versus 7.8 per 1000 catheter-days in the control group ($P = .02$).

Conclusions. In the present study, application of cloxacillin as antibiotic lock solution for dialysis catheters resulted in a considerable reduction in catheter-related bacteremia rate.

IJKD 2011;5:328-31
www.ijkd.org

INTRODUCTION

Double-lumen catheters are vital for achieving immediate vascular access. They are primarily used for dialysis treatment of acute kidney failure in bed-bound patients and as a short-term substitute malfunctioning permanent access. Long-term use of nontunneled noncuffed catheters is not recommended, but in practice, it does occur with acceptable infection rates in dialysis centers where tunneled cuffed catheters are not available. Most of our patients in dialysis centers of Shiraz, Iran, have been using noncuffed, nontunneled catheters and they needed it at least until their arteriovenous fistula could be used for dialysis.

Infectious complications resulting from catheter

use in the hemodialysis population remain the significant cause of morbidity and mortality in this population. Because conservation of vascular access sites remains a therapeutic mainstay for long-term hemodialysis patients, clinical investigators have evaluated the safety and efficacy of catheter preservation with antimicrobial lock solutions, instilled into the lumens of catheters to treat and prevent infectious complications.¹ Reduction in the rates of major complications such as infection and thrombosis that limit the lifespan of hemodialysis catheters could conceivably lead to improved survival of temporary nontunneled catheters.

The clinical features of catheter-related blood stream infection are generally indistinguishable

from those of blood stream infections arising from other foci of infections²; most patients develop fever and chills which may be accompanied by hypotension, hyperventilation, altered mental status, and nonspecific gastrointestinal manifestations such as nausea, vomiting, abdominal pain, and diarrhea. Some patients have signs of local infection (inflammation or frank purulence) at the exit site of the catheter.³ The infection risks associated with temporary double-lumen catheters include local exit site infection and systemic bacteremia, both of which require prompt removal of the catheter and appropriate intravenous antibiotic therapy. Bacteremia generally results from either contamination of catheter lumen or migration of bacteria from the skin through the entry site, down the hemodialysis catheter into the blood stream. This usually limits the duration of use of these catheters. *Staphylococcus* and *Streptococcus* species are responsible for the majority of infections. An important element in the development of catheter-related bacteremia is biofilm formation; biofilm is not present at the time of placement of a new catheter, but it is formed relatively soon thereafter. Biofilm formation facilitates the attachment of microorganisms to the surface of the catheter. It has been recognized that once the organism is embedded in the biofilm matrix, they become relatively resistant to antibiotics.⁴

The objectives of this study were to evaluate utilization of an antimicrobial lock solution (cloxacillin and heparin) in temporary noncuffed double-lumen catheters for long-term intermittent hemodialysis as a method of preventing catheter-related infection.

MATERIALS AND METHODS

In this clinical trial, we included 100 prevalent hemodialysis patients with a newly inserted jugular subclavian or femoral uncuffed catheter. They were on dialysis in Nemazi Hospital, Saadi Hospital, and Sadra Hospital, in Shiraz, Iran, selected randomly from the eligible population between 2007 and 2008. The study protocol was approved by the local ethics committee, and the participants provided written consent. Adult patients on long-term hemodialysis (twice or three times per week), regardless of the cause of kidney failure, with newly inserted uncuffed temporary double-lumen catheters were included

in this trial. Participants were randomly divided into 2 groups. In the study group, the patients received a solution containing cloxacillin, 100 mg/mL, plus heparin, 1000 IU/mL; a 2.5-mL injection of the solution was instilled in each of catheter lumens by the personnel of the dialysis units, and the catheters were allowed to dwell until the next session of dialysis. In the control group, the participants received an instillation of 2.5 mL of a solution composed of heparin and normal saline in each lumen of the temporary noncuffed catheters after each dialysis session, as it is done routinely in these dialysis centers.

All of the patients were followed for 6 months, and their conditions were checked through weekly telephone calls. Medical records of patients admitted for double-lumen catheter infection were collected. In those suspected for infection, 2 BACTEC aerobic plus media blood cultures (BD diagnostics, New Jersey, USA) were taken from the catheter site and the opposite hand peripheral for demonstration of catheter-associated infection. Samples were placed on chocolate blood agar for 48 hours after 5 days in the BACTEC device 924. Data including age, underlying disease, type of central venous catheter, date of catheter insertion, signs and symptoms of infection, duration of hospitalization, and cost of hospitalization were collected to be compared between the two groups.

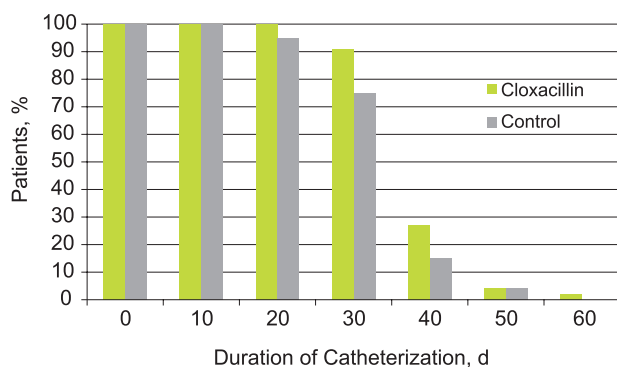
The Student *t* test, the chi-square test, and the Fissure exact test were used for analysis of comparisons between the two groups, as appropriate. The Kaplan-Meier method was applied to estimate the infection-free survival time of the catheters. The SPSS software (Statistical Package for the Social Sciences, version 14.0, SPSS Inc, Chicago, Ill, USA) was used for data entry and analysis. A *P* value less than .05 was considered significant.

RESULTS

Fifty patients received heparin only (22 women and 28 men), and 50 received heparin and cloxacillin (28 women with 22 men). The Table shows characteristics of the patients in the two groups. In patients receiving heparin and cloxacillin, 1 catheter-related infection was observed; he was a 56-year-old diabetic man with right-sided double-lumen in the subclavian vein, hospitalized for 10 days. He was discharged from hospital without any complications, after catheter removal and insertion

Characteristic of Hemodialysis Patients With and Without Cloxacillin Antibiotic Lock Solution

Parameter	Cloxacillin Group	Control Group
Number of patients	50	50
Mean age, y	50.1	52.3
Female, %	56	44
Diabetes mellitus, %	40	42
Mean duration of catheterization, d	35.0 ± 2.0	32.5 ± 2.5



Percentage of patients who maintained their catheters.

of a new catheter in the other side. Significant colonization of the catheter hub occurred in 8 cases of patients treated with heparin and saline solution, all of whom admitted to hospital and the catheters were removed (mean duration of their hospitalization, 8 days). The organisms that caused catheter hub colonization were *Staphylococcus epidermidis* (6 patients) and *Staphylococcus aureus* (2 patients).

The rate of catheter-related bacteremia (CRB) was 0.5 per 1000 catheter-days in the study group and 7.8 per 1000 catheter-days in the control group ($P = .02$). The mean CRB-free catheter survival was 35 days (95% confidence interval, 33 to 37 days) in the study group and 32.5 days (95% confidence interval, 30 to 35 days) in the control group (Figure). The risk reduction rate of infection was 7% (95% confidence interval, 6.4% to 7.6%) when cloxacillin solution was used as a substitute for heparin alone.

DISCUSSION

In 1961, Shaldon, Chiandussi, and Higgs introduced temporary hemodialysis catheters, and these catheters continued to be the primary means of achieving acute hemodialysis access.²⁻⁴ The questions for clinicians are what is the risk of bacteremia and how long should catheters remain

in place before the risk is too high.⁵ Our prospective study found a bacteremia rate of 7.8 per 1000 catheter-days, which is similar to other prospective studies of temporary catheters that range from 3.9 to 9.7 bacteremia episodes per 1000 catheter-days.^{6,7} Most of the new hemodialysis patients in Shiraz dialysis units used uncuffed catheter, and thus, they were exposed to a greater risk of infection. In the present study the control group showed a 16% incidence of CRB. However the application of cloxacillin resulted in a considerable reduction in CRB rate (0.5 events per 1000 catheter-days).

Cloxacillin is known not to have adverse effects when administered 3 times a week and is not considered to cause a problem, because antibiotics act in the lumen of the catheters, and even in the case of leakage, antibiotics were present at low dose. Antibiotic lock technique in patients using uncuffed catheter may be a low-cost means of reducing incidence of CRB in patients in whom it is practically difficult to place a tunneled cuffed catheter for temporary vascular access during maturation of arteriovenous fistula. However, widespread use of antibiotic lock technique may not be ideal because of the emergence of the antibiotic-resistant organisms.⁷ A recent study comparing taurolidine lock with standard heparin lock reported effective reduction of the infection; thus, taurolidine-containing catheter lock solution may be an alternative strategy for preventing emergence of antibiotic-resistant bacteria. In a study by Saxena and Panhorta,⁷ the authors evaluated the impact of the locking of a broad-spectrum antibiotic, cefotaxime, with heparin on the incidence of catheter thrombosis, catheter-related blood stream infection, and the nontunneled catheter life span. Their results showed a lower catheter-related blood stream infection incidence (1.65 per 1000 catheter-days in cefotaxime group versus 3.13 per 1000 catheter-days in no-cefotaxime group). In the case of gentamicin, about 10% of patients complained of symptoms compatible with aminoglycoside ototoxicity.^{5,8}

CONCLUSIONS

Our clinical trial shows that an antibiotic lock technique with cloxacillin can decrease the frequency of catheter-related gram-positive bacterial infection in patients with uncuffed double-lumen catheters for temporary vascular access during arteriovenous

fistula maturation. This prophylactic strategy can be a basis for conducting future randomized trials with other antibiotics.

CONFLICT OF INTEREST

None declared.

ACKNOWLEDGEMENTS

This work was accomplished in collaboration with the Nephrology Investigation Center of Shiraz University of Medical Sciences and the Microbiological Investigation Center of Dr Alborzi.

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Received October 2009
Revised March 2011
Accepted April 2011

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