The effect of single dose prophylactic vancomycin before semi-permanent catheterization to prevent catheter related infection; a randomized controlled trial, phase II

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A B S T R A C T

Introduction: Catheter-related infections are a common complication and a major cause of morbidity and mortality in hemodialysis patients with tunneled central venous catheters. The optimal strategy for the management and prevention of catheter-related infections is unclear.

Objectives: This study is aimed to evaluate the single-dose prophylactic vancomycin efficacy before semi-permanent catheterization to prevent catheter-related infection.

Patients and Methods: This randomized double-blind controlled clinical trial was conducted on patients with chronic renal failure requiring hemodialysis and insertion of a double-lumen central venous catheter admitted to Ahvaz Golestan Hospital. The intervention group (n=30) received 1 g of vancomycin intravenously one hour before catheter insertion and the control group (n=30) received an equal amount of normal saline. The incidence of catheter-related infections and other complications for 6 months was evaluated.

Results: During the 6-month follow-up, hospitalization due to catheter-related infection and the need for antibiotic administration was observed in 9 patients (30.0%) who received vancomycin and 14 patients (46.7%) in the control group (P=0.184). Catheter extraction due to infection was observed in 4 patients of the vancomycin group (13.3%) and 6 patients of the control group (20.7%) (P=0.451). Complications other than infection were observed in four patients (13.3%) in each group (P=1.000). The mean time to onset of infection was 2.43 ± 0.38 months in the control group and 3.85 ± 0.42 months in the vancomycin group (P=0.002).

Conclusion: Although a single dose of intravenous vancomycin one hour before insertion of a bi-luminal hemodialysis catheter did not show a significant effect on preventing catheter-related infections over 6 months, it significantly delayed the onset of infection.

Trial Registration: The trial protocol was approved by Iranian Registry of Clinical Trial (Ethical code: IR.AJUMS.HGOLESTAN.REC.1399.106 and IRCT code: IRCT20201206049617N1; https://www.irct.ir/trial/52832).

Implication for health policy/practice/research/medical education:
The requirement for hemodialysis is increasing worldwide with the rate of patients suffering from end-stage renal disease. Hemodialysis catheterization is accompanied by several complications including catheter-related infections, which has an effect on patients’ mortality and morbidity and is a huge economic burden on patients and society. One of the techniques to prevent this complication is antibiotics, which may be able to lower the expenses on the medical care systems.

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Introduction
The rate of patients suffering from end-stage renal disease (ESRD) is increasing worldwide and these patients need renal replacement therapy (RRT) for improved survival. Hemodialysis is the most common RRT in use (1). Hemodialysis tunneled catheters are easily applicable devices to access the central vein and are commonly used in patients with chronic kidney disease undergoing hemodialysis (2,3). However, insertion of these catheters is followed by several complications including catheter-
related infections, which are the most common secondary complication of hemodialysis catheterization and are correlated with significant mortality and morbidity and are considered a huge economic burden on patients and society (4,5). Several techniques are recommended including disinfecting the catheter site and the use of locking solutions containing heparin, antibiotics and hypertonic substances to prevent these complications (6,7).

Recently, numerous studies are focused on the antibiotic consumption to prevent important catheter-related complications and loss of expenses on medical care systems (7,8). Most catheter-induced infections are caused by gram-positive organisms including *Staphylococcus aureus*, which is the cause of 50 to 84% of these cases (9). Thus, empirical therapy is mostly based on coverage of gram-positive cocci, and glycopeptide antibiotics such as vancomycin or teicoplanin are considered in the treatment of catheter-induced infections (10).

Moreover, even though using antibiotic locking solutions has been shown effective in preventing hemodialysis catheter-related infections (7,11). Conversely, guidelines still do not support the routine use of prophylactic antimicrobial locking solutions (2). In one study on patients suffering from malignancy, prophylactic vancomycin infusion before central venous catheterization post-bone-marrow transplant was assessed and it was observed that the infection rate was 6% in the vancomycin group and 55% in the control group (12).

**Objectives**

Due to a limited number of studies on the efficacy of prophylactic vancomycin infusion in preventing catheter-related infections, and also due to contradictory results from previous studies on this topic (13), our current study was designed and conducted to assess the efficacy of prophylactic antibiotic (vancomycin) before semi-permanent catheterization to prevent catheter-related infections.

**Patients and Methods**

**Study design**

The current study is a randomized, double-blind, placebo-controlled clinical trial that was conducted on chronic kidney failure patients, admitted to the nephrology ward in Golestan Hospital, Ahvaz University of Medical Sciences, in the years 2020-2021. All procedures were performed following the Helsinki declaration and informed written consent was obtained from all study patients before the start of treatment.

Adult ESRD patients in need of permanent dialysis and bi-luminal catheterization in jugular veins in sterile conditions, were included in the study. Exclusion criteria were: history of antibiotic use in the previous month, having permanent or semi-permanent catheters on other body sites, and active infection in the previous month.

The study flow-chart is presented in Figure 1.

Since there were no similar studies on this content, our study is a phase II clinical trial, thus there was no need to determine the sample size, and 30 patients were enrolled in each group as samples. Sampling was done by convenient method.

Randomization was done by the department secretary who was blind to the study, and was done by the

**Figure 1. Study flow-chart.**

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<table>
<thead>
<tr>
<th>Patients undergoing hemodialysis in need of semi-permanent catheterization admitted to Ahvaz Golestan Hospital (n=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excluded patients (n=16):</td>
</tr>
<tr>
<td>- Patient’s unwillingness (n=4)</td>
</tr>
<tr>
<td>- Active infection (n=5)</td>
</tr>
<tr>
<td>- Antibiotic use in the previous month (n=7)</td>
</tr>
<tr>
<td>Enrollment</td>
</tr>
<tr>
<td>Randomization (n=60)</td>
</tr>
<tr>
<td>Vancomycin (n=30)</td>
</tr>
<tr>
<td>- Catheter-related infection (n=9)</td>
</tr>
<tr>
<td>- Other complications (n=4)</td>
</tr>
<tr>
<td>Treatment Agent</td>
</tr>
<tr>
<td>Normal Saline (n=30)</td>
</tr>
<tr>
<td>- Catheter-related infection (n=14)</td>
</tr>
<tr>
<td>- Other complications (n=4)</td>
</tr>
<tr>
<td>Follow-up</td>
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<tr>
<td>Analysis</td>
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<tr>
<td>Result Analysis (n=30)</td>
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<td>Result Analysis (n=30)</td>
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random block permutation method with a block size of 4, and patients were randomly assigned to two groups. Patients in the intervention group received a dose of 1g intravenous vancomycin, an hour before semi-permanent catheterization. Patients in the control group received the same amount of normal saline by a personnel blind to the study groups. Vials containing normal saline were similar to vancomycin vials; the labels were obliterated and were relabeled as vials 1 and 2; the color and volume of agents were identical. Patients and personnel who assessed the results were blind to randomization of patients into two intervention and control groups and the study was performed double-blinded. An experienced interventionist inserted the catheters, using a face mask, gown, sterile gloves, and sterile drapes. No infectious sites were detected in patients before enrollment in the study. The catheterization site was disinfected with betadine and covered with a sterile drape. After each dialysis, the catheter exit site would be disinfected with betadine and recovered with gauze. To ensure the patency of the catheter, after every dialysis, each lumen would be filled with 3500 units of diluted heparin and the catheter would only be used for hemodialysis.

Severity and time to onset of infection and other catheter-related complications including catheter dysfunction, bleeding from the catheter and deep vein thrombosis (DVT), were assessed within 6 months. Diagnosis of catheter-related infection was based on blood culture, catheter’s lumen culture, and symptoms such as fever, chills and purulent discharge from the catheter site, and was assessed by a resident of Internal Medicine, participating in the study. For this purpose, the patients were visited and assessed each week during the study and if any infection-related symptoms were reported, a complete physical examination would be performed and laboratory tests such as complete blood count (CBC), urinalysis, blood culture, catheter’s lumen culture and pulmonary X-ray would be obtained. If it was necessary to extract the catheter, the distal 2 cm of the removed catheter would be aseptically excised, and immediately sent for culture assessment. In case of erythema and purulent discharge in the catheter’s exit site, or in case of fever with no other origin, the catheter would be extracted. We should note that the necessary follow-up guidelines were offered to the patients in a written form.

**Statistical analysis**

For statistical analysis, version 22 of SPSS software (SPSS Inc., Chicago, IL, U.S.A) was used. For quantitative variables, we used mean values and standard deviations, and for qualitative variables, we used frequency and percentage values. The normal distribution of variables was assessed by the Shapiro-Wilk test. For data analysis, independent *t* tests and chi-square tests were used. A *P* value of 0.05 was considered the level of significance.

**Results**

The basic characteristics of participants of the two groups are shown in Table 1. As shown, participants were not significantly different in terms of age and sex.

Table 1. Basic characteristic of participants in two groups

| Variables                      | Control (n=30) | Vancomycin (n=30) | *P* value * 
|--------------------------------|----------------|-------------------|--------------
| Age (years), mean ± SD         | 54.41 ± 10.91  | 51.88 ± 11.448    | 0.355        
| Gender, No. (%)                |                |                   | 0.795        
| Female                         | 16 (53.3)      | 17 (56.7)         |              
| Male                           | 14 (46.7)      | 13 (43.3)         |              

* Chi-square test (comparing sex frequency) and independent *t* test (comparing mean age) between two groups.

Table 2. Comparison of intervention between two groups of vancomycin and control

| Variable                                          | Control group (n=30) | Vancomycin group (n=30) | *P* value *
|---------------------------------------------------|----------------------|-------------------------|------------
| Fever and chills during or after dialysis         | 17 (56.7)            | 10 (33.3)               | 0.069      
| Erythema and inflammation in the catheter site   | 18 (60.0)            | 13 (43.3)               | 0.196      
| Purulent discharge from the catheter lumen       | 14 (46.7)            | 9 (30.0)                | 0.184      
| Time to onset of infection - months               | 2.43 ± 0.38          | 3.85 ± 0.42             | 0.002      
| Number of participants receiving outpatient antibiotics for catheter infection | 14 (46.7) | 10 (33.3) | 0.292 |
| Duration of receiving outpatient antibiotics - months | 2.96 ± 0.41          | 4.08 ± 0.68             | 0.001      
| Number of hospitalizations due to catheter infection and antibiotic therapy | 14 (46.7) | 9 (30.0) | 0.184 |
| Duration of hospitalization due to infection – months | 4.78 ± 0.58          | 4.19 ± 0.95             | 0.083      
| Non-infectious complications                     | 4 (13.3)             | 4 (13.3)                | 1.000      
| Catheter replacement                              | 6 (20.7)             | 4 (13.3)                | 0.451      
| Death                                            | 4 (13.3)             | 3 (10.0)                | 0.688      

* Chi-square test (comparing frequency of values) and independent *t* test (comparing mean values) between two groups

Numbers are shown as either mean ± SD or frequency (%) values
groups of vancomycin and control. Infection symptoms such as fever and chills during or after dialysis, erythema, and inflammation in the catheter site, and purulent discharge from the catheter lumen and also the number of hospitalizations due to catheter infection and antibiotic therapy in the vancomycin group were less than the control group, but this difference was not statistically significant. The time to onset of infection was $2.43 \pm 0.38$ months in the control group, and $3.85 \pm 0.42$ months in the vancomycin group, and this difference was statistically significant ($P = 0.002$). Other complications were observed in 4 patients in each group: 2 cases of catheter dysfunction and 2 cases of bleeding in the vancomycin group; 3 cases of catheter dysfunction, 1 case of DVT; and 1 case of bleeding in the control group. In this study, 3 cases of death were reported in the vancomycin group (2 cases due to COVID infection and 1 case due to catheter infection) and 4 cases of death were reported in the control group (1 case due to COVID-19 infection, 1 case due to cancer, 1 case due to heart failure, and 1 case due to catheter infection).

**Discussion**

In our study, in a period of 6-month follow-up, hospitalization due to catheter-related infection and the need for antibiotic therapy were observed in 14 patients (46.7%) in the control group and 9 patients (30.0%) in the vancomycin group. The high rates of catheter-related infections observed in our study show the need for more precise precautions and disinfection techniques. Furthermore, despite hospitalization and antibiotic therapy, about 1/6th of the cases needed catheter replacement (13.3% of cases in the vancomycin group and 20.7% in the control group). Even though our study was not able to show that 1g intravenous vancomycin infusion an hour before semi-permanent hemodialysis catheterization in comparison with normal saline infusion (control group), had a significant effect on preventing catheter-related infections, yet vancomycin was able to delay onset infection; as shown, the mean time to development of infection was $2.43 \pm 0.38$ months in the control group and was $3.85 \pm 0.42$ in the vancomycin group. This difference was statistically significant.

We need to note that in our study, instead of using an antibiotic locking solution and infusion of the antibiotic in the catheter site, we used the prophylaxis in the form of systemic antibiotic infusion to prevent catheter-related bloodstream infection (CRBSI), which has a high prevalence in such patients. Most catheters are colonized with environmental bacteria and the colonized pathogenic micro-organisms in the catheter can easily form a bacterial biofilm which can be spread in the bloodstream and develop CRBSI (14). Thus the risk for the development of hemodialysis catheter-related infection is considerable. Since both the treatment of catheter-related infection and hospitalization and the resulting catheter replacement are costly and correlated with different complications, thus precautions to prevent infection, are necessary. These results are consistent with our study, even though the infusion modality and follow-up duration were different from ours.

In another study by Mavromatidis et al (13), it was reported that a 500 mg infusion of vancomycin via a peripheral vein, had no significant effect on preventing hemodialysis catheter-related infection; likely, the study’s low dose of vancomycin and the infusion via a peripheral vein were causes of the inefficacy observed. A meta-analysis was performed, assessing the efficacy of prophylactic use of different antibiotics such as vancomycin, teicoplanin, or ceftazidime in preventing gram-positive infections due to long-term central venous catheters in cancer patients; this meta-analysis showed that neither of the administration of the antibiotic before catheterization had any advantages over prescribing them. But it seems that the use of antibiotics with heparin as a locking solution for long-term Central venous catheters, decreases rates of catheter-induced gram-positive sepsis in patients with the risk of neutropenia during chemotherapy or disease. Also in this study, it was concluded that since the use of antibiotics and heparin combination may increase antibiotic resistance, thus it must be considered only in patients with a high risk of infection or with an early severe infection of the central venous catheter (15). In a study by van de Wetering et al, (16) on patients with oncologic complications, it was reported that infusion of systemic vancomycin/teicoplanin before central venous catheter insertion to decrease catheter-related infections, was not significantly effective in comparison with the control group. Therefore, even though our study shows that vancomycin is able to prevent infection symptoms in short-term, but regarding lack of significant difference in infection rate in 6 months between the two groups and also the result of other similar studies, prescribing vancomycin empirically and in long-term to prevent bacterial resistance to *Staphylococcus aureus*, as was reported by Global Antimicrobial Resistance Surveillance System (GLASS), is not recommended (17,18). in a prospective study by Vassilomanolakis et al (12) in 1995, the efficacy of prophylactic 500 mg vancomycin infusion in 3 doses before catheterization in patients with central venous catheters after bone-marrow transplant was assessed and it was observed that infection rate in 30 days after transplant in the prophylactic vancomycin group (6%) was significantly lower than the control group (55%). In a prospective study by Al-Hwiesh and Abdul-Rahman (11), it was reported that an antibiotic locking solution (combination of gentamycin 45 mg/mL and vancomycin 25 mg/mL) for preventing hemodialysis catheter-related infection, is effective. In this study, the catheter-related infection rate in 1 year was reported at 4.54 cases per 1000 hemodialysis sessions in the antibiotic group and 13.11 cases per 1000 hemodialysis sessions in the control group. In a randomized, controlled clinical trial conducted by Gadallah et al (19), it was reported that...
prescribing a single dose of intravenous vancomycin (1 g), 12 hours before permanent catheterization in patients undergoing peritoneal dialysis, resulted in decreased acute peritonitis risk after catheterization. In this study, patients were followed for 12 days. But the group receiving cefazolin in comparison with the control group, did not show significant decrease in prevention of infection (19).

In another study, Huddam et al (20), assessed efficacy of a single dose of intravenous antibiotic before catheterization in order to prevent catheter-related infection in patients undergoing hemodialysis and reported that 1 g of cefazolin in comparison with normal saline resulted in a significant decrease in catheter-related infections, bacteremia and catheter failure in patients undergoing hemodialysis.

Of reasons contributing to the different results between studies, may be the difference in basic characteristics of participants, dosage and form of antibiotic prescription, and the duration of the follow-up period. Since no study assessed the efficacy of prophylactic infusion of single-dose intravenous vancomycin in the prevention of catheter-related infections in patients undergoing hemodialysis, therefore it is not possible to precisely compare our results with previous studies. Still, according to our results, even though vancomycin administration resulted in a lower catheter-related infection rate, in comparison with the control group, the difference was not statistically significant.

**Conclusion**

Although our results in 6 months could not show that in patients suffering chronic renal failure who need semi-permanent catheters, vancomycin infusion before venous bi-luminal catheterization has a protective role against catheter-related infection and other catheter-related complications compared to normal saline, vancomycin significantly delayed the time to onset of the infection. Furthermore, the rate of infection and hospitalization due to infection in the vancomycin group was lower than in the control group, but this difference was not statistically significant.

**Limitations of the study**

In the end we must note that this controlled, clinical trial was the first assessment done on the efficacy of prophylactic single-dose intravenous vancomycin administration to prevent semi-permanent catheter-induced infection in hemodialysis patients and showed valuable results. However, our study had some limitations, including:

- Since our study was conducted over a long period of 6 months and the infection rate probably increases in the upcoming weeks following the decrease in the vancomycin effect, therefore vancomycin may have prevented infection in a short-term period.
- In our study, the organism causing the catheter-

-induced infection was not assessed and identified.

- Of other study limitations, we can name the low number of participants in each group.

Therefore, by conducting more studies with larger sample size and deployment of multiple centers, better results will be achieved.

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**Authors’ contribution**

AA, ZZ, AG and SAH were the principal investigators of the study. AA, ZZ, AG, and SAH were included in preparing the concept and design. AA and ZZ revisited the manuscript, and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

**Conflicts of interest**

The authors declare that they have no competing interests.

**Ethical issues**

Ethical issues including plagiarism, data fabrication, and double publication have been completely observed by the authors. The research was conducted following the tenets of the Declaration of Helsinki. The Ethics Committee of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran approved this study (IR.AJUMS.HGOLESTAN.REC.1399.106). Accordingly, written informed consent was taken from all participants before any intervention. The present article is based on a student’s internal medicine residency thesis with the research project code CRD-9909, at Ahvaz Jundishapur University of Medical Sciences. The trial protocol was approved by the Iranian registry of clinical trial (IRCT code: IRCT20201206049617N1; https://www.irct.ir/trial/52832).

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**References**

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