J Nephropharmacol. 2022; x(x): e10489.

http://www.jnephropharmacology.com DOI: 10.34172/npj.2022.10489

Journal of Nephropharmacology

Evaluating risk factors for catheter-related infections in hemodialysis patients

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ARTICLE INFO

Article Type:
Original

Article History:
Received: 2 February 2022
Accepted: 30 May 2022
Published online: 9 June 2022

Keywords:
Catheter-related Infection
End-stage kidney disease
Hemodialysis
Iron
Ferritin

ABSTRACT

Introduction: Catheter-related infection in the patients with end-stage renal disease (ESRD) is one of the leading causes of death. Identifying risk factors for infection, including patients' iron profile, plays an important role in preventing this complication.

Objectives: In this study, we aimed to determine the risk factors of catheter-related infections among the ESRD patients in Qazvin, Iran.

Patients and Methods: In this observational study, 41 patients with hemodialysis venous catheter-related infection (case group) and 42 patients without catheter-related infection (control group) in Qazvin educational and medical centers were studied. The definition of functional iron deficiency anemia included ferritin <500 ng/mL and serum iron/total iron-binding capacity (TIBC) <30%. The laboratory evaluation method was based on enzyme-linked immunosorbent assay method. Definition of catheter-related infection in this study consisted of two positive results of the three cultures from blue and red catheter lines and blood at the same time with the same microorganism.

Results: In studying iron parameters, a significant difference between serum iron levels and transferrin saturation in the two groups was detected (*P* values of 0.0016 and 0.003, respectively). Both parameters were higher in the control group. The most common microorganism causing the infection was Staphylococcus aureus (43.9%) and most of the catheters used were of temporary internal jugular vein types. The most important risk factors in the incidence of catheter infection were diabetes mellitus (OR = 5.059) and high serum iron levels (OR = 1.053). Decreased transferrin saturation levels reduced the risk of infection (OR = 0.825).

Conclusion: There was a relationship between iron profile and diabetes mellitus and the increased risk of catheter-related infections. To prevent infection, patients with ESRD undergoing hemodialysis with venous catheters, blood sugar and serum iron levels need to be monitored carefully and iron overdose should be prevented in these patients.

Implication for health policy/practice/research/medical education:
In an observational study, we evaluated the risk factors for catheter-related infection in end-stage chronic renal failure patients undergoing hemodialysis and found that diabetes mellitus and excess serum iron levels are two major risk factors. In addition, lower-serum transferrin saturation could be a protective agent.

Please cite this paper as: Hajian S, Seifzade M. Evaluating risk factors for catheter-related infections in hemodialysis patients. J Nephropharmacol. 2022;x(x):e10489. DOI: 10.34172/npj.2021.10489.

Introduction

Hemodialysis can be conducted in three ways; arterial venous fistula (AVF), central venous catheters and grafts. Previous studies show that hemodialysis through an intravenous arterial fistula or graft is associated with longer survival and hospitalization than hemodialysis through the venous catheters (1).

Recent data show that 15%-50% of patients with end-stage renal disease (ESRD) in Europe and 60% of these patients in the United States begin their hemodialysis program with central venous catheters (2). The incidence of catheter infection and bacteremia in hemodialysis patients is estimated to be 0.4-4.5 and 0.2-3.9, respectively, per 1000 days of catheter implantation (3). Central venous catheters are a major risk factor for bacteremia in hemodialysis patients, which can cause life-threatening complications in more than 10% of cases, including septic shock, endocarditis, septic arthritis, osteomyelitis and epidural abscesses. The relative risk of hospitalization for infection and death is 2-3 times higher in the patients using central venous catheters than in the patients using AVF or grafts (4).

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Infection is the second leading cause of death after cardiovascular diseases in hemodialysis patients (5,6). Definition of catheter-related infection consists of two positive results from the three cultures of blue and red catheter lines and blood at the same time with the same microorganism. The method of accessing blood vessels for hemodialysis is the main risk factor for bacteremia in hemodialysis patients, which is ten times higher than the AVF method if venous catheters are used. Identifying risk factors for infections associated with central venous catheters is effective in preventing their occurrence. These risk factors in various studies included catheter placement site and time, type of catheter, previous history of catheter infection, recent surgical history, iron overload, Staphylococcus aureus colonization within the nose, older age, diabetes mellitus, low-hemoglobin and albumin levels (7-9).

According to the KDIGO guideline, functional iron deficiency anemia includes ferritin <500 ng/mL and serum iron/ total iron-binding capacity (TIBC) <30%(10).

Iron deficiency anemia causes numerous complications among hemodialysis patients such as heart disease, infection, weakness, decreased quality of life and restless leg syndrome, showing the prevalence at 59% among this group (11).

Iron deficiency may increase the risk of infection because this nutrient is needed for the normal functioning of the immune system. Iron is an essential factor for the bactericidal activity of macrophages and is a part of the structure of peroxidase and nitrous oxidase enzymes (12). In addition, it is effective in the count and function of T lymphocytes (13). Reciprocally, according to the studies, iron is an essential nutrient for many pathogens (14). Some studies have shown that iron has a negative effect on the bactericidal activity of macrophages. In contrast, other studies have shown iron overload may promote infection (15). Prevention and treatment of catheter infections in hemodialysis patients is critical as a major cause of mortality and morbidity.

Objectives

The aim of the present study was to evaluate of risk factors for catheter-related infections in hemodialysis patients in Qazvin province.

Patients and Methods

Study design

In this observational study, 41 patients with ESRD who had permanent or temporary catheters for hemodialysis, and underwent catheter and blood culture diagnostics due to catheter infection as well as 42 patients with ESRD who were not confirmed to have catheter infection were examined for the association between catheter infection and iron deficiency anemia (Figure 1).

Case and control groups were matched in terms of gender and age ratios. This study was conducted for one year from April 2018 to March 2019 in the educational and medical centers of Qazvin province.

The definition of functional iron deficiency anemia included ferritin <500 ng/mL and serum iron/TIBC<30%;

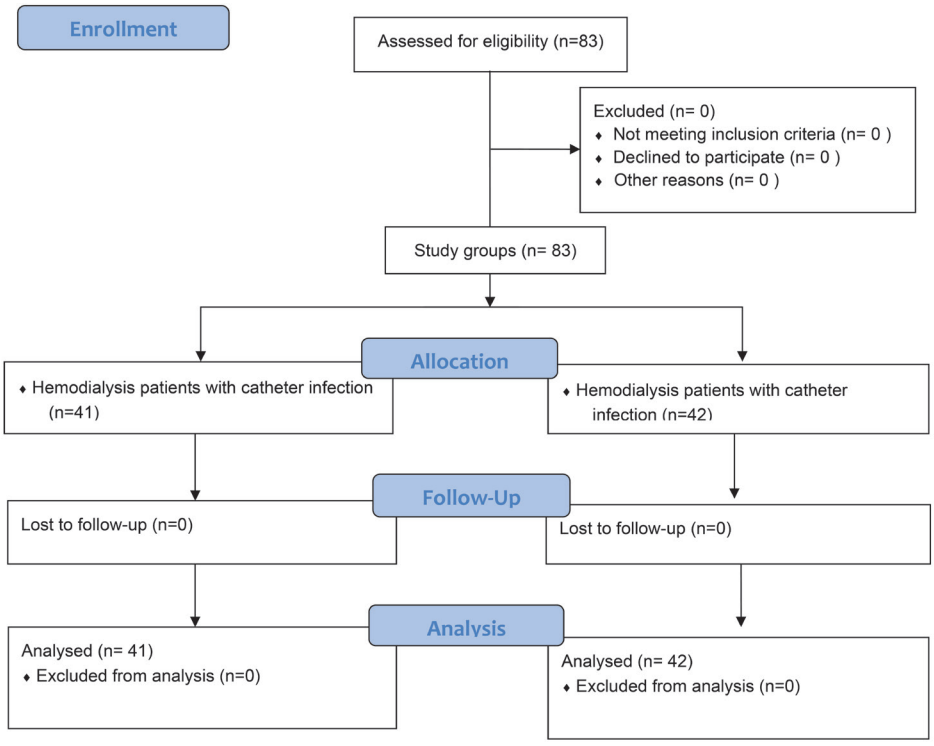

Figure 1. Flow diagram of the study.

the laboratory evaluation method was based on enzyme-linked immunosorbent assay method. Groups with and without catheter infection were evaluated in terms of albumin status, diabetes mellitus, catheter location and type of catheter for permanent or temporary and duration of catheter implantation; then, the data were analyzed by a statistical consultant. Inclusion criteria included all the hemodialysis patients who had permanent or temporary catheters and, according to the diagnostic criteria, catheter infection was proven in them. The control group included the hemodialysis patients who had permanent or temporary catheters and did not have catheter infection. Exclusion criteria were the patient's dissatisfaction with participating in the study.

Statistical analysis

In order to obtain the sample size in this study, the results of the study by Jones et al (16) that ferritin levels were obtained in the patients with and without catheter infection were conducted. Then, using G*Power 3.0.10 software, the sample size was obtained based on the mean and standard deviation of ferritin in the control and case groups. With the first type error of 5% ($\alpha = 0.05$) and test power of 80% ($\beta = 0.2$), the sample size was estimated to be at least 40 people per group.

In this study, SPSS software (version 23) was conducted to analyze the data. Mean and standard deviation were employed to describe the numerical data. Cross-table and chi-squared test were employed to describe and analyze the qualitative data. T-test and Kolmogorov–Smirnov test were utilized to analyze the numerical quantitative data with normal distribution. We used binary logistic regression test to examine the odds ratio of different risk factors for infection.

Results

In this study, 83 patients with ESRD and undergoing hemodialysis with permanent or temporary catheters (mean age of 59 years old) were retrospectively reviewed. Forty patients were male and 43 patients were female, which included 48.2% and 51.8% of them, respectively. In addition, 42 patients were in the control group and 41 patients in the case group. Of these, 41 patients had diabetes mellitus, which included 49.4% of the total patients.

Most of the patients in this study had internal jugular catheters (59%) and temporary type (66.3%). The rest of the patients had permanent type and femoral catheters.

Based on the study of cultures from blood as well as red and blue lines of catheter of the patients, the most common organism was Staphylococcus aureus, which grew in 18 patients (43.9%) in the culture media (Table 1).

Chi-square test was conducted to compare the qualitative and demographic data between the two groups.

The number of male and female patients in the control group was 23 (54.8%) and 19 (45.2%), respectively. In the case group, the number of men and women was 17 (41.5%) and 24 (58.5%), respectively.

Table 1. Frequency of causative microorganisms of catheter-related infection (N=41)

Organism	Number of patients
Staphylococcus aureus	(43.9%) 18
Staphylococcus epidermidis	(17.1%) 7
Pseudomonas aeruginosa	(22%) 9
Escherichia coli	(4.9%) 2
Acinetobacter	(4.95) 2
Klebsiella pneumonia	(2.4%) 1
Enterococci	(2.45)1
Gram positive bacilli	(2.4%) 1

Moreover, 31% of patients in the control group and 68.3% of patients in the case group had diabetes mellitus; in the analysis, the difference between the two groups in terms of diabetes mellitus was significant (P <0.05).

Around 52.4% of the patients in the control group and 65.9% of the case group had a jugular catheter and the rest in the two groups had a femoral catheter.

In this study, the most common catheter used in the patients was temporary catheters.

To compare the quantitative statistical data obtained from the two groups, univariate T-test analysis was used. Based on the results, the mean age of the control and case groups was 58 and 59 years old, respectively, without statistically significant differences.

The mean of hemoglobin in the control and case groups was 9.82 g/dL and 10.17 g/dL, respectively. In the analysis of the data related to patients' iron profiles, the mean serum iron levels in the control and case groups were 63.17 µg/dL and 60.93 µg/dL, respectively, TIBC 260.4 µg/dL and 303.9 µg/dL, transferrin saturation percentage 25.36% and 19.53%, respectively, and ferritin 578.26 ng/mL and 497 ng/mL, respectively.

There was a statistically significant difference between the TIBC and transferrin saturation percentage between the variables related to the patients' iron profiles (P < 0.05). In comparing the mean albumin of the two groups, the level of serum albumin in the control group was 3.66 g/dL and, in the case group, it was 3.52 g/dL (Table 2).

To investigate the odds ratio and significance level of the variables, we used binary logistic regression analysis. In this study, a statistically significant relationship was observed between catheter infection and serum iron level, transferrin saturation percentage and diabetes mellitus (Table 3).

Discussion

Catheter-related infections are among the main and increasing causes of mortality and morbidity and cost for the medical system of countries in hemodialysis patients dependent on venous catheters (17,18).

In our study, diabetes mellitus was examined as a possible comorbidity of increased risk of infection in individuals in

Table 2. Comparing statistical data between patients with and without catheter-related infection

Parameters	Case group (with catheter related infection)	Control group (without catheter related infection)	*P* value
Number of patients	41	42	
Age (y), Mean±SD	59±14	58±15	0.8
Gender			0.2
Male	17 (41.5%)	23 (54.8%)	
Female	24 (58.5%)	19 (45.2%)	
Diabetes mellitus	28 (68.3%)		0.001
Location of catheter			0.2
Jugular	27 (65.9%)	22 (52.4%)	
Femoral	14 (34.1%)	20 (47.6%)	
Type of catheter			1
Temporary	27 (65.9%)	28 (66.7%)	
Permanent	14 (34.1%)	14 (33.3%)	
Hb (g/dL), Mean±SD	10.17±2.31	9.82±2.57	0.5
Serum iron (µg/dL), Mean±SD	60.93±31.72	63.17±39.85	0.7
TIBC (µg/dL), Mean±SD	303.9±52.74	260.4±61.12	0.001
Transferrin saturation (%), Mean±SD	19.53±7.97	25.36±15.44	0.03
Ferritin (ng/mL), Mean±SD	565.12±339.8	578.26±357.9	0.3
Albumin (g/dL), Mean±SD	3.52±0.82	3.66±0.45	0.3

Hb: hemoglobin, TIBC: total iron binding capacity.

both groups. It should be noted that 31% of the control group and 68.3% of the case group had diabetes mellitus, which was statistically significant. The most important risk factor for catheter infection in hemodialysis patients was diabetes mellitus with OR = 5.059. In contrast to our results, in many studies in this field, the prevalence of diabetes was not significantly different between the case and control groups (16,19-22). However, in the study by Martin et al (20) similar to ours, diabetes mellitus was the most important risk factor for catheter infections after implantation in the internal jugular vein. In some other studies, a significant relationship has been reported between the control and case groups for diabetes mellitus (8,21).

The most common microbial pathogen causing catheter infection in our study was Staphylococcus aureus. This organism was responsible for causing infection in 43.9% of the infected patients. In all other similar studies, the most common organism causing the infection was Staphylococcus aureus. In various studies, the share of Staphylococcus aureus has varied from 23% to 97% (16,19,20,22).

In our study, the mean duration of catheter retention until infection was 144 days and the median was 120 days.

Table 3. Binary regression analysis of risk factors for catheter-related infection

Parameters	Odds ratio	P value
Serum iron	1.053	0.016
Transferrin saturation	0.825	0.006
Diabetes mellitus	5.059	0.002

In a similar study, this time was 25 days in people with complicated catheter infection and 50.5 days in people with uncomplicated infection (19). The mean duration of catheter retention until infection occurring in the study by Jones et al (16) was clearly longer than in our study which was at 214.5 days.

In this study, we performed a complete study on iron profile in all patients in the control and case groups. In the study by Nabi et al (22), unlike our study, the level of serum iron was higher in the case group. The mean serum iron levels in the control and case groups were 16.5 µg/dL and 22.6 µg/dL, respectively, indicating a lower serum iron level in the patients of this study than in our work. There was no significant relationship between serum iron levels of the two groups. The study by Jones et al (16) also examined serum iron levels in the patients with and without catheter infection undergoing hemodialysis. In their study, contrary to our study, serum iron levels were higher in the patients with infection. Serum iron levels were clearly higher in our study. The mean serum iron level in the patients with catheter infection in this study was 17 µg/dL and, in non-catheter infection patients, it was 12 µg/dL. Similar to our study, no significant relationship between the two groups in terms of serum iron levels were detected.

Our investigation is one of the few studies that examined other parameters of iron profile such as TIBC, ferritin and transferrin saturation. Among similar studies, only the study by Jones et al examined the parameters of iron profile. Jones et al only examined the serum ferritin level in the control and case groups. The results were inconsistent with the findings of our study. In this study, the mean

serum ferritin level in the patients with catheter infection was 834 ng/mL, and in non-infectious group, it was 459 ng/mL. Similar to our study, no significant difference was observed between the groups.

Conclusion

Based on the findings of this study, diabetes mellitus and higher serum iron levels put hemodialysis patients with venous catheters at increased risk for venous catheter infection. Lower levels of transferrin saturation in these patients reduce the risk of infection.

There was no difference between permanent and temporary venous catheters as well as femoral and jugular insertion for catheter infection. Therefore, it is recommended that, in all the patients with end-stage renal failure undergoing hemodialysis with venous catheters, blood sugar and serum iron levels be carefully monitored. This factor reduces the risk of infections associated with venous catheterization as an important cause of mortality in hemodialysis patients. Avoiding excessive iron intake can effectively reduce the risk of infection due to the increased percentage of transferrin saturation.

Accordingly, further researchs in this field is recommended to investigate the role of invasive therapies in controlling blood glucose and serum iron levels in reducing the risk of venous catheter infections in the patients with ESRD undergoing hemodialysis.

Limitations of the study

Some of our study limitations included small sample size, single-center and short period of study. The use of a larger sample size, multicenter designs and longer periods for data collection could increase the value of information.

Authors' contribution

SH and MS were the principal investigators of the study. SH and MS prepared the concept and design. SH revisited the manuscript and critically evaluated the intellectual contents. Both authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. Both authors read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Ethical issues

The research conducted in accordance with the tents of the Declaration of Helsinki. The Ethics Committee of Qazvin university of medical sciences approved this study. The institutional ethical committee at Qazvin university of medical sciences accepted all study protocols (IR.QUMS.REC.1396.445). Accordingly, written informed consent was taken from all participants. This study was part of internal medicine residential thesis of Moosa Seifzade at this university (Thesis #111193).

Conflicts of interests

The authors declare that they have no conflict of interest.

Funding/Support

The authors declared no receipt of the following financial support for the research, authorship, and/or publication of this article.

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