Infection-Related Hospitalizations in Home Hemodialysis Patients

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Key Words

Infection · Hospitalization · Home hemodialysis ·
Daily hemodialysis

Abstract

Introduction and Aims: Infection is an important cause of hospitalization and death in patients receiving hemodialysis (HD). Few studies have examined infection-related hospitalizations in home HD (HHD) population. The purpose of this study was to examine the scope of infections and the effect of HHD modality (daily home HD (DHD) and conventional home HD (CHD)) on infection-related hospitalizations in HHD patients. **Methods:** The study was performed in a large cohort of HHD patients. Infection-related hospitalizations during July 1, 2005, and August 30, 2010, were abstracted from the centralized computer system. Data on demographics, dialysis vintage and dialysis modality were analyzed. **Results:** One hundred sixty-five patients were included. During a median follow-up of 5 years, infection-related hospitalizations were observed in approximately 35.8% of all hospitalizations, which was the first cause for hospitalization. Rates of non-access-related infections were observed to be higher than that of access-related infections (1.7:1). Rates (per 100 person-years) of soft-tissue infection, pneumonia and sepsis ranged from 0.85 to 1.82 in patients on HHD. Meanwhile, access-related infection was the main cause for access-related hospitalizations (34.8%). Cox regression analysis showed

that the usage of different dialysis modalities was not associated with a high risk for infection-related hospitalizations in HHD patients. **Conclusions:** Infection-related hospitalization occurred frequently in HHD patients. A broad range of infections, many unrelated to dialysis access, resulted in hospitalization in this population. HHD modalities were not associated with infection-related hospitalizations in HHD patients. Video Journal Club 'Cappuccino with Claudio Ronco' at <http://www.karger.com/?doi=433517>.

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Infection is a frequent cause of hospitalization in patients with end-stage renal disease (ESRD) and is the second leading cause of mortality after cardiovascular disease [1–4]. Although overall hospital admission rates have been stabilized in the ESRD population at approximately 2 hospitalizations per patient per year, the rate of infection-related hospitalizations has increased by nearly 26% between 1993 and 2007 [5]. The infection-related hospitalizations rates for a national sample of 332,442 adult incident dialysis patients were reported to be similar to 35% [6].

Because of the recognition that infections contribute substantially to the morbidity and mortality of patients on dialysis therapy, most attention has focused on bacte-

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remia and peritonitis, complications of hemodialysis (HD) and peritoneal dialysis access, respectively [6–9]. Most reported studies are retrospective and have identified diabetes, older age, comorbidity, hypoalbuminemia and the use of a temporary dialysis catheter as the major independent risk factors for infections [10–14].

However, few studies have examined infection-related hospitalizations in home HD (HHD) population. HHD is an important renal replacement therapy in ESRD patients. HHD can provide more frequent and/or increased duration of dialysis, which are believed to be more physiological and better tolerated by patients than thrice weekly conventional HD (CHD) [15, 16]. Whether infections contribute substantially to the morbidity of patients on HHD is unknown. Furthermore, because infection-related hospitalizations are potentially preventable [17], it is important to assess the frequency and associated risk factors to improve patient care in the HHD population.

We, therefore, conducted this study to explore the scope of infections and the associated risk factors on infection-related hospitalizations in HHD patients.

Methods

Patient Population

The HHD program in Northwest Kidney Centers, University of Washington, Seattle, was started in 1967. Patients were considered to be appropriate candidates if they were physically able to perform HD 5–6 days each week at home. Data was collected and a retrospective cohort study was performed on all the patients who were under HHD treatment between July 1, 2005 and August 30, 2010, and had no history of kidney transplant. Patients with prior kidney transplants were excluded to avoid capturing transplant-related infections and those related to possible ongoing immunosuppression, which would increase the risk of infection. We followed up the cohort until death, kidney transplant or study end on August 30, 2010.

Most patients in our program were using daily home HD (DHD), 5–6 times per week, 3–3.5 h each time. Some patients were using nocturnal home HD (NHD), 4–6 times per week, 6–8 h each time and CHD, 3 times a week, 4 h each time. For DHD and NHD, the NxStage System machine (NxStage Medical Inc.) was used, a system that requires much slower dialysate flow rates. Some of them used the PureFlow machine (NxStage medical Inc.) for preparation of a 60-l batch of dialysate that could be used for a maximum of 3 home treatments. Patients on CHD used the B-Braun machine.

Data Source and Data Collection

We reviewed the centralized computer system for our health-care organization and recorded all hospital admissions that occurred in patients who performed HHD, including their respective total length of stay. We also recorded the primary admitting diagnosis, as well as any secondary diagnoses, that could have been related to the diagnosis of ESRD. Data for patients' age, vintage

from the first HHD treatment, sex, race, cause of kidney failure and dialysis modality were also examined.

Infection-related hospitalizations were examined after the first 90 days of dialysis therapy to minimize the number of patients changing dialysis modality (because a large percentage of patients change dialysis modality in the first 90 days of dialysis therapy) [1]. Infection-related hospitalizations included hospitalizations for septicemia, bacteremia, endocarditis, pulmonary infections (e.g. viral pneumonia, bacterial pneumonia, influenza with respiratory manifestations and abscess of lung or mediastinum), genitourinary infections (e.g. urinary tract infection, pyelonephritis and perinephric abscess), gastrointestinal infections (e.g. diverticulitis, *Clostridium difficile* colitis, perirectal abscess and cholecystitis), peritonitis, soft-tissue infections (e.g. cellulitis, necrotizing fasciitis and gangrene) and joint or bone infections (e.g. infective arthritis and osteomyelitis) [1]. We examined all the discharge diagnoses for each hospitalization, and participants were classified as having an infection-related hospitalization if any of the discharge diagnoses included an infection of interest. Therefore, we defined infection-related hospitalizations as hospitalizations for which infection was either the primary reason for hospitalization or a secondary complication of hospitalization.

Statistical Analysis

Continuous variables are expressed as means $\pm$ SD, and categorical variables are expressed as ratios or percentages. Comparisons of mean values were performed by the 2-tailed Student's *t* test for unpaired values. Comparisons of ratios or percentages among groups were performed by the χ^2 test.

We examined the number of infection-related hospitalizations per patient and number of infection-related diagnoses per hospitalization. Multiple infection-related diagnoses per hospitalization were captured for each patient, and all hospitalizations during follow-up were examined for infection-related diagnoses. To calculate the rates of each type of infection (e.g. pulmonary, genitourinary and gastrointestinal), the number of hospitalizations within a specific infection category were divided by the total person-time of follow-up.

We examined overall rates of infection-related hospitalization during follow-up. To examine whether rates differed over time, we further examined rates of infection-related hospitalizations in 3-month intervals. Risk factors for infection-related hospitalization were evaluated using an extension of the Cox proportional hazards model. All analyses were conducted using SPSS software (version 16.0). A *p* value <0.05 was considered to be statistically significant.

Results

A total of 165 prevalent dialysis patients were included in the cohort. As described in other cohorts, patients on HHD therapy tended to be younger and were more likely to be white and male (table 1).

Admitting diagnoses and associated lengths of stay (days spent in the hospital) are listed in table 2. We observed 176 admissions in our HHD population. Median follow-up was 5 years; infection-related hospitalizations were observed in approximately 35.8% of all hospitalizations in patients who

were on HHD treatment, which was the first cause for hospitalization. Surgical reasons and access problems were the second and third cause for hospitalizations, separately.

During the follow-up, approximately 40.6% patients on HHD were hospitalized, while 21.8% patients had at least 1 infection-related hospitalization (i.e. ≥ 1 infection-related discharge diagnosis), that is, 15.1% patients had 1 infection-related hospitalization and 6.7% patients had ≥ 2 infection-related hospitalizations.

We identified a wide range of infections, including sepsis, access-related infection, pulmonary, gastrointestinal and soft-tissue infections. Rates of non-access-related infections were observed to be higher than that of access-related infections (1.7:1). During follow-up, patients on HHD therapy experienced 49 infection-related hospitalizations (overall rate, 5.94 events/100 person-years). Rates (per 100 person-years) of specific infection-related hospitalizations were 1.82 for septicemia, 1.09 for pneumonia, 0.85 for soft-tissue infection, 0.61 for access-related infection and 0.36 for gastrointestinal infections in patients on HHD (fig. 1). Meanwhile, access-related infection was the main cause for access-related hospitalizations (34.8%).

In patients on HHD therapy, rates of infection-related hospitalizations (per 100 person-years) were 1.82 for months 3 through 12 months, 1.09 for months 12 through 24 months, 1.21 for months 24 through 36 months, 0.36 for months 36 through 48 months, 1.08 for months 48 through 60 months of follow-up (fig. 2).

Table 3 lists the demographic data in infection-related hospitalization group and non-hospitalization group. There were 36 and 98 patients in these 2 groups, respectively. Age, race, etiology and diabetes mellitus (DM) percentage in these 2 groups were similar ($p > 0.05$). The percentage of DHD use in the infection-related hospitalization group was lower than that in the non-hospitalization group. However, there was no significant difference in NHD and CHD use in those 2 groups.

In the Cox proportional hazards model, age, sex, race, DM and modality use were put into the analysis of the model. DM was associated with a 40% increase of infection-related events in HHD patients (hazard ratio (HR) 1.40, 95% CI 1.26–2.83). All the other factors did not reach statistical significance ($p > 0.05$; table 4).

Discussion

In our study of HHD patients, we found that infection-related hospitalization occurred frequently and was the first cause for hospitalization. A broad range of infections,

Table 1. Demographic data of the study population (n = 165)

Characteristic	n (%)
Age, years, mean $\pm$ SD	50.8 $\pm$ 15.6
Sex, male	113 (68.5)
DM	67 (40.6)
Dialysis vintage, months, mean $\pm$ SD	70.8 $\pm$ 77.9
Modality	
DHD	110 (66.7)
NHD	15 (9.1)
CHD	40 (24.2)
Etiology of uremia	
DM	52 (31.5)
Chronic glomerulonephritis	36 (21.8)
Hypertension	21 (12.7)
Polycystic kidney disease	13 (7.8)
Others	43 (26.1)
Race	
White	98 (59.4)
Black	35 (21.2)
Asian	17 (10.3)
Others	15 (9.1)

Table 2. Admitting diagnoses and associated lengths of stay

Diagnosis	Admissions, n (%)	Mean hospital days
Non-ESRD related		
Pulmonary disease	3	2.0
Cardiac disease	11	17.5
Gastrointestinal disease	10	6.1
Gynecological disease	3	1.7
Infections	49	5.8
Peripheral vascular disease	8	19.4
Fall	1	4.0
Surgical disease	24	5.3
Cancer	3	15.6
Other	7	7.3
Total non-ESRD related	119 (67.6)	798.6 (75.0)
ESRD related		
Fluid disturbance	11	5.1
Electrodisturbance	5	1.8
Access problem	23	5.9
Gastrointestinal bleeding	7	5.0
Other (anemia)	5	2.3
No record	6	3.2
Total ESRD related	59 (32.4)	266.5 (25.0)
Total	176	1,065.1

Fig. 1. Types and rates of infection-related hospitalizations.

Fig. 2. Distribution of the number of infection-related hospitalizations.

many unrelated to dialysis access, resulted in hospitalization in this population. Higher rates of specific non-access-related infections (e.g. pneumonia and sepsis) were observed in HHD patients compared to access-related infections. Meanwhile, HHD modality was found not to be associated with infection-related hospitalizations in HHD patients.

To our knowledge, this is the first study to examine the burden of infection in HHD population. Our findings reinforce the importance of understanding that patients on HHD therapy experience a high burden of infection-related complications and emphasize that dialysis patients are at high risk of acquiring a number of infections.

In our study, infection-related hospitalization was defined as any hospitalization in which infection was the

principle diagnosis, or a secondary complication of hospitalization, in prevalent HHD patients [6]. Our result showed that, during 5 years of follow-up, infection-related hospitalization was found to be 35.8% of all hospitalizations in HHD patients and was the first cause for hospitalizations. The result is similar to that in the study by Dalrymple et al. [1]. In their study, they investigated the infection-related hospitalization in older patients with ESRD. They found that during the 2 years of follow-up, infection-related diagnoses were observed in 34 and 36% of all hospitalizations in incident patients on HD and peritoneal dialysis therapy, respectively.

Meanwhile, we found that a spectrum of infections contributed to infection-related hospitalizations, especially non-access-related infections. A wide range of in-

Table 3. Demographic comparison between infection-related hospitalization and non-hospitalization group

Parameter	Infection-related hospitalization (n = 36)	Non-hospitalization (n = 98)	p value
Age	51.4±17.8	54.8±16.3	0.87
Male	24 (67.7)	67 (68.4)	0.91
DM	15 (41.9)	34 (34.7)	0.29
Dialysis vintage	28.1±54.5	26.4±50.1	0.39
Race			
White	24 (67.8)	56 (57.1)	0.11
Non-white	12 (32.2)	44 (42.9)	0.11
Etiology			
Diabetes	13 (35.5)	30 (30.6)	0.45
Glomerulonephritis	9 (25.8)	20 (20.4)	0.57
Hypertension	2 (6.5)	14 (14.3)	0.10
Other	12 (33.3)	34 (34.6)	0.76
Modality			
DHD	23 (64.5)	78 (79.6)	0.01
NHD	6 (16.1)	7 (7.1)	0.05
CHD	7 (19.4)	13 (13.3)	0.24

Data are presented as mean ± SD or number (%).

Table 4. Multivariable Cox regression models of factors associated with the risk of infection-related events in patients on HHD

	HR	95% CI	p value
Age, years			
<60	1.00	ref.	
≥60	1.28	0.54–3.00	0.56
Male	0.66	0.28–1.57	0.35
Race			
White	1.00	ref.	0.63
Non-white	0.82	0.38–1.79	
Diabetes	1.40	1.26–2.83	0.03
Modality			
CHD	1.00	ref.	
DHD	1.28	0.74–5.31	0.17

fections including sepsis, pneumonia, gastrointestinal and soft-tissue infections and access-related infection were found in our study. Rates of non-access-related infections were observed to be higher than those of access-related infections (1.7:1). The broad range of infections in this study was similar to that in older patients with ESRD in the study by Dalrymple et al. [1]. These findings suggest that there is a lower immune level in dialysis population, and dialysis patients experience a high burden of infec-

tion-related complications beyond those related to dialysis access. Meanwhile, the result in the study reported that in peritoneal dialysis patients, rates of specific infection-related hospitalizations (per 100 person-years) were 10.6 for septicemia, 10.3 for pulmonary, 4.7 for gastrointestinal and 8.8 for soft-tissue infections. Compared to their study results, our results were significantly lower, which may to some extent be explained by the much younger age of the patients in our study as older age was a high risk factor for infections.

Our results showed that infection-related hospitalizations during the first 12 months after initiation of HHD are highest and decreased over the later 4 years. This result is similar to those in the studies by Chavers et al. [6] and Lafrance et al. [17]. The US Renal Data System annual report also suggested that admission rates were higher in the first year of dialysis [7]. During the first year of dialysis, patients are believed to be at greater risk of morbidity than that in subsequent years [7], possibly because of greater use of catheters in that period after adjustment of dialysis regimens [18]. This phenomenon may also be explained by survival effect: patients with severe concurrent conditions will die early, whereas healthier patients remain on dialysis longer. Because patients with more comorbidities are admitted to hospital more often, rates of admission would be higher in the first years when those patients are still in the cohort [17].

Many factors such as older age, diabetes, heart failure, pulmonary disease, inability to ambulate, low serum albumin level and cancer have been associated with an increased risk of specific or overall infections in previous studies of patients on dialysis therapy [10, 19–21]. In our study, DM was also found to be associated with a nearly 40% increase of infection-related events in HHD patients. Patients with DM have a high risk for infections. In agreement, HEMO Study also confirmed an increased risk of serious infectious events among diabetic patients than among non-diabetic patients on HD [4]. More comorbidities are easily found in DM patients than in non-DM patients, which may also contribute to the high risk for infections.

Although we found that the percentage of DHD use in the non-hospitalization group was significantly higher than that in the infection-related hospitalization group in our study, in the Cox proportional model, HHD modality was found not to be associated with infection-related hospitalizations in HHD patients. The negative result in the Cox proportional model was possibly due to the small sample size. There were only 36 patients in the infection group in the present study; this may limit the statistical power. In the study by Ting et al. [22], the researcher

strongly demonstrated that DHD can improve hospitalization (admission rates and hospital days) compared to CHD. Furthermore, many studies have reported that DHD could significantly improve patient quality of life, functional status and clinical outcomes, such as improved nutrition status, and possibly decreased infection-related hospitalizations [23]. In DHD, solute and fluid fluctuations are less extreme and peak toxin levels are lower because interdialytic intervals are shorter. Treatments are more continuous. This characteristic of less 'unphysiology' in DHD itself may be related with better clinical outcome compared to CHD [24–28].

Our study had several limitations. First, baseline data for comorbid conditions were unavailable because of the limitation of the centralized computer system, which may influence the risk estimates of comorbid illnesses to infections. Second, information on some potential confounders, such as serum albumin and serum C-reactive protein, was not available. Third, the study was conducted at a single center with a small sample size. We did have 36 patients in the infection group in this cohort, which may influence the statistical power to some extent.

In summary, findings from our study show that infections are very common in the HHD patients, and they

were the first cause for hospitalization in this population. A broad range of infections, many unrelated to dialysis access, resulted in hospitalization in this population. HHD modality was not associated with infection-related hospitalizations in HHD patients. Given the high rates of infection-related hospitalizations and importance in HHD patients and the potential cardiovascular consequences of infection in patients on dialysis therapy, we need to better understand the infectious disease-related complications and develop effective preventive and treatment strategies for this population.

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Disclosure Statement

The authors have no conflicts of interest to declare.

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