Chapter 8

Prevention and Management of Nosocomial Pneumonia in Hemodialysis Patients

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1. Introduction

Infectious disease is one of the main complications in the patients on long-term hemodialysis. Various clinical features, including multiple comorbidities, frequent hospitalization, and immunosuppression, rendered these patients susceptible to nosocomial infections. Furthermore, hemodialysis frequently results in chronic wasting, inflammation, uremia and gastrointestinal disturbances, all of which contribute to the increasing frailty of the patient. In their weakened state, these patients are susceptible to infectious complications such as aspiration pneumonia. In this section, we discuss these aspects of hemodialysis based on the recent our clinical observations.

1.1. Background of infectious disease in maintenance hemodialysis patients

Infectious diseases are significant causes of morbidity and mortality among patients with end-stage renal disease (ESRD), which is ranked as the second leading cause of death in Japanese maintenance hemodialysis (MHD) patients, following cardiovascular diseases. An increased susceptibility to infections has been ascribed partly to old age, a high prevalence of diabetes, defective phagocytic function of granulocytes, and frequent exposure to potential infectious risk factors during the hemodialysis therapy including endotoxin [1]. Anemia and malnutrition also contribute to the immune-compromised status of MHD patients. In addition, MHD patients are suffering from protein-energy wasting (PEW), making them susceptible to sarcopenia due to increased muscle protein degradation. Malnutrition causes impaired immune function and poor wound healing.

In addition, MHD patients usually have problems other than infections, such as cardiovascular or muscle-skeletal disorders. These patients are frequently hospitalized for surgical procedures or reasons other than infection, where they were treated with various kinds of antibiotics over a long period. These typical clinical courses undergone by MHD patients are known to influence the clinical characteristics and microbiological features of pneumonia.

2. PEW and Frailty in MHD patients

As MHD patients get older, they are affected more severely by age-related problems as compared to their counterparts in the general population. Two of the most significant problem are frailty and protein energy wasting (PEW) [2]. This phenomenon is clinically relevant because many manifestations of frailty and PEW are strong risk factors that affect quality of life, morbidity, and mortality. Frailty can be defined as a biological syndrome of decreased resistance to stressors caused by cumulative declines across multiple physiological systems which, ultimately, results in vulnerability to adverse outcomes. Frailty implies decreased body energy, protein reserves and reduced strength. Frailty is a common occurrence in CKD as well as MHD patients. A simple criterion for frailty can be the presence of three or more of the following abnormalities; unintentional weight loss, self-reported exhaustion, measured weakness, slow walking speed, and low physical activity. On the other hand, PEW is defined as the loss of somatic and circulating body protein and energy reserves. The comorbidity of infectious disease is also subject to the influence of these conditions. For instance, sarcopenia and osteopenia puts the patient at risk for falls as well as contracting pneumonia. In regards to aspiration pneumonia (AP), sarcopenia often causes difficulty in swallowing, which leads to unrecognized aspiration. Coordinated muscle movement and optimal muscle strength play an important role in the well-organized swallowing movement. Aspiration status was partly dependent on the lower anterior and posterior esophageal muscle and tongue strength [3]. These muscle strength was imparired by the decline in the global physical status. In ESRD patients under MHD, muscle and energy wasting are prominent, which influences the mortality and morbidity [2]. The tissue changes in muscle varies from morphological, electrophysiological and metabolic alterations. These malign changes of muscles lead to muscle weakness and finally to myopathy [4]. Additionally, atrophy of type II fibers was observed in the patients with MHD in several studies. These functional and structural muscle impairments in both systemic and/or oropharyngeal muscle strength are derived from the PEW state in MHD patients. Impaired immune function is associated with PEW in MHD [5]. In addition to an increased susceptibility to infections and poor wound healing, PEW leads to an impaired immune function which affects the gastrointestinal tract malfunction and aberrant microbiota population. These intestinal changes cause malabsorption and malnutrition [6], accelerating further the immune dysfunction. Deterioration in intestinal structure also leads to the enhancement of bacterial translocation in the intestine, leading to systemic inflammation and PEW state.

PEW involves several mechanisms, including the activation of oxidative stress, the inflammatory response, and the dialysis measure itself. Several markers of PEW and the resultant

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malnutrition have been associated with the incidence and death rates in patients with MHD [2]. Biochemical markers like lower serum albumin, prealbumin and cholesterol levels [7] are linked to malnutrition with higher fatality in dialysis patients. Serum transferrin, creatinine and bicarbonates [8] as well as hemoglobin levels, lymphocytes counts and white blood cell counts are also shown to be associated with malnutrition. We previously reported that serum creatatinine, albumin and total cholesterol levels are independent risk factors for contracting AP and its corresponding mortality rate. We also identified serum inorganic phosphorus (IP) as the main predictors of dietary intake in MHD patients [9]. Since 24-hour creatinine excretion and serum creatinine levels are associated with muscle mass [10], creatinine decline over time are related to the level of malnutrition as well as sarcopenic changes after admission [10]. It was reported that, in a cohort of 121,762 MHD patients, serum creatinine decline, and lower body mass, lower muscle mass and weight loss are associated with higher mortality in MHD patients [11]. It was also reported that among these clinical parameters, a decline in serum creatinine is suggested to be a stronger predictor of fatality than weight loss in MHD patients [12]. Our study is in consistent with the results of this large cohort study in that creatinine decline rate as well as albumin decline rate are good predictive indicator for morbidity and mortality of AP [9].

3. Respiratory infection in hemodialysis

Pneumonia is the second most common cause of severe infection in the MHD population. Regarding infectious diseases, it has been reported that approximately 20% of infectious deaths in MHD patients are attributed to pneumonia. The mortality of pulmonary infections in MHD patients has been reported to be 14 to 16 times higher than in the general population [13]. *Streptococcus pneumonia*, seasonal influenza and bacterial pneumonia secondary to influenza have been leading causes for community-acquired pneumonia in MHD. A vaccination is available for the prevention of pneumonia from *Streptococcus pneumonia as is same with the case in* the general population. Current guidelines recommend the vaccination of all MHD patients and revaccination after 5 years since a more rapid decline in the antibody titer was observed compared to that of the general population.

4. Nosocomial pneumonia

We surveyed 1803 MHD patients admitted to our university hospital between April 2001 and March 2007 [14]. We investigated basic patient characteristics and clinical characteristics of nosocomial pneumonia. The distribution of patient age indicated that about 70% of the patients were over 60 years old. The average length of hospitalization was 28.1 days, ranging from one day to 478 days, which was longer than the average for our hospital (14.2 days). Patients were admitted to different departments for a variety of reasons. We isolated 391 microorganisms from the sputa of 138 patients that were suspected of respiratory tract infections. These include *Candida albicans (C. albicans)*, methicillin-resistant *Staphyloccocus aureus* (MRSA), and *Staphy-*

loccocus epidermidis which were the leading three isolates. Among these patients, 47 were diagnosed with pneumonia and 57 pathogens were isolated. From the sputa specimen of pneumonia patients, MRSA and *C. albicans* were most frequently isolated. *Stenotrophomonas maltophilia* (*S. maltophilis*) was also isolated and found to be resistant to older generation cephalosporins, carbapenems, and quinolones. However, new fluoroquinolones, such as levofloxacin, were found to be affective. Among the 138 patients suspected of respiratory tract infections, 15 out of 23 patients infected with *S. maltophilia* died, resulting in the highest mortality among all patients with nosocomial pneumonia examined. With this survey, we concluded that MHD patients suffered from nosocomial pneumonia with multi-drug resistant pathogens. Consequently, *S. maltophilia*-related infections are associated with a high mortality rate and should be taken very seriously.

5. AP in MHD patients

Of the different types of pneumonia, AP is of particular interest due to its recent increase in occurrence in the aged MHD population. Aged patients are susceptible to dysphagia caused by neurological dysfunctions due to cerebral infarctions, cognitive deficits, and muscle weakness. Since HD patients are susceptible to sarcopenia and malnutrition, these changes increases the risk of development of AP. We recently reported on the clinical characteristics of AP in MHD patients [9]. We surveyed consecutive MHD patients with nosocomial AP who were admitted to our university hospital between April 2007 and December 2008. We determined hospitalized MHD patients as a high-risk population for AP, and we revealed that the mortality rate of HD patients with AP was high. We analyzed the risk factors for AP and found that the rate of decline of serum creatinine and albumin levels indicative of the decrease in muscle mass and malnutrition were of predictive value for the contraction of AP. We also found that he AP patients fed via nasal tube feeding or oral intake tended to survive.

6. Management of nosocomial pneumonia

Based on the clinical backgrounds, MHD patients suffered from nosocomial pneumonia with multi-drug resistant pathogens. Significantly, we reported that *S. maltophilia*-related infections should be taken seriously due to the associated high mortality rate. In addition, we stressed the clinical importance of AP for MHD patients suffering from PEW. Various treatment options to prevent AP were advocated, including oral hygiene, altered food viscosity, and positioning [9]. Medications for this purpose include angiotensin-converting enzyme inhibitors and amantadine. In our study, early initiation of tube feeding appears to provide more favorable outcomes in light of intestinal conditions or fluid restrictions in HD patients. Parenteral nutrition directly affects the total body fluid volume and is prone to volume overload as compared to tube feeding. In addition, malnutrition and sarcopenia lead to silent aspiration where the symptoms are not always clinically evident. Since hospitalized patients with hemodialysis often progress to a state of malnutrition, the patients should be considered to have silent aspiration and treated with tube feeding.

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7. Conclusions

Various backgrounds including multiple comorbidities, PEW or frailty, impaired immune response, infectious diseases and pneumonia were prevalent in MHD patients. Our surveillance revealed that MHD patients suffered from nosocomial pneumonia with multi-drug resistant pathogens. *S. maltophilia*-related infections should be very seriously in light of the associated high mortality rate. Based on the PEW condition, both the contraction and mortality rates of nosocomial AP were high among HD patients.

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