Current Status of Dialysis Therapy and Related Clinical Guidelines in Japan

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Tadao AKIZAWA*1

As of the end of 2008, the number of prevalent patients on dialysis in Japan was approximately 283,000 (2,213 per million population, PMP), a rise of 2.7% over the previous year. Similarly, the number of incident patients on dialysis is on the increase, reaching approximately 38,000 (296 PMP), a rise of 2.1% over the previous year. The background of dialysis patients is characterized by aging (the average age of prevalent patients is 65.3 and that of incident patients is 67.2), and increasing cases of diabetic nephropathy/nephrosclerosis as the primary disease. Patients with diabetes mellitus and those with nephrosclerosis represent 34% and 7% of all prevalent patients, and 43% and 11% of all incident patients, respectively. In contrast to these patients, the proportion of prevalent patients on dialysis for chronic glomerulonephritis has been decreasing. Since the number of older patients and patients with severe arteriosclerotic, diabetic nephropathy/nephrosclerosis, whose prognosis is poor, is increasing, it is anticipated that the prognosis of dialysis population may deteriorate. The annual crude mortality rates in dialysis patients, however, has basically been constant around 9.5%, and both 1- and 5-year survival rates (82% and 59%, respectively) show a slightly improving tendency.[1] The results of Dialysis Outcomes and Practice Pattern Study (DOPPS) also revealed that the prognosis of dialysis patients in Japan was better than that in the U.S. or Europe, and that such a good prognosis, and the static situation concerning renal transplantations (the annual number of transplantations in 2008 was 1,201), are partly responsible for the growing number of patients receiving dialysis in this country. Owing to the static situation concerning renal transplantations and the good prognosis, the number of patients who are controlled by dialysis on the long term has increased. The duration of dialysis therapy is prolonged to 10 years or more in nearly 70,000 patients and 20 years or more in nearly 20,000 patients, with a maximum duration of 40 years and 8 months. Heart failure is always the most common cause of death among dialysis patients and is responsible for approximately 24% of deaths, followed by infections and malignant neoplasms, and then cerebrovascular disorders and myocardial infarction. These causes of death reflect the aging of society and the increase in diabetes as the primary disease. Deaths due to cardiovascular diseases exceeded 40% of all deaths, indicating that increased cardiovascular risks in dialysis patients is the reflection of the terminal stage of chronic kidney disease, which is the representative risk factor of cardiovascular disease.

Although the prognosis of dialysis patients in Japan is the best in the world, their life expectancy is markedly low, namely less than 50% of the general population, irrespective of age at which dialysis therapy is started. Prolonged dialysis therapy is often accompanied by specific complications, such as dialysis-related amyloidosis and mineral bone disorders, which cause extreme deterioration in the QOL of the patients. The Japanese Society for Dialysis Therapy (JSDT) has proposed various clinical guidelines to maintain the high levels of dialysis therapy to improve the life prognosis and QOL of patients. The representative guidelines are explained below.

Management of Anemia

The first guideline was established in 2004[2]

*1 Chairman of the Japanese Society for Dialysis Therapy; Division of Nephrology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan (akizawa@med.showa.ac.jp).

targeting only hemodialysis patients. The guideline sets the target hemoglobin (Hb) value at 10–11 g/dL (or at 11–12 g/dL for relatively young patients with mild arteriosclerotic lesion and high activity levels). In 2008, the scope of the guideline was expanded to peritoneal dialysis, and patients with chronic renal failure in the conservative stage, and the target Hb value was determined to be from 11 g/dL to <13 g/dL (or <12 g/dL for patients with cardiovascular complications, etc.). The guideline also provides a full explanation of the method of using erythropoiesis stimulating agents (ESAs), the diagnostic criteria for iron deficiency, the method of iron replacement, and the measures for poor responder to ESAs.[3]

Management of Secondary Hyperparathyroidism

The guideline[4] published in 2006 provides a full explanation of the criteria for and the method of the management of abnormalities in serum calcium (Ca) and phosphorus (P), and secondary hyperparathyroidism, which occurs frequently in dialysis patients. The guideline sets the target ranges of serum P, Ca and intact PTH at 3.5–6.0 mg/dL, 8.4–10.0 mg/dL and 60–180 pg/mL, respectively (as pre-hemodialysis values). These target ranges were determined by reanalyzing the JSDT data base and trying to set the ranges depending as much as possible on the best survival rates. Among these parameters, a higher priority should be given to maintenance of serum P and then the serum Ca should be corrected within the target range. If secondary hyperparathyroidism with an intact PTH exceeding 500 pg/mL remains although serum P and Ca levels are controlled within the target ranges, parathyroidectomy should be considered. In response to the launching of cinacalcet in 2008, the guideline is undergoing minor revisions to include the method of using cinacalcet.

Vascular Access Construction and Repair

Ninety-five percent of hemodialysis patients in Japan have vascular access (VA) as the most preferable form, arterio-venous fistula (AVF). This is considered to be partially responsible for the good prognosis of regular hemodialysis patients in this country. The guideline published in 2005[5] provides a full explanation of the timing of VA construction, AVF, arterio-venous graft (AVG), catheters, the selection, construction and management of the superficialization of an artery, the method of monitoring VA function, and the timing and policy of repair, etc., and strongly recommends the early construction of AVF in preparation of the introduction of dialysis.

Peritoneal Dialysis

Approximately 96% of dialysis patients in Japan are on hemodialysis and fewer than 4% of the patients undergo peritoneal dialysis (PD). The guideline published in 2009 to achieve the appropriate proliferation of PD in Japan provides a full explanation of the timing of starting PD, the selection and construction of peritoneal access, the practical introduction of PD, the method of measuring peritoneal function and dialysis dose, the proper prescription of PD, nutrition management, and the discontinuation criteria to avoid encapsulating peritoneal sclerosis, as well as the concept of "PD first" and "PD last." This guideline is also useful to clarify the difference in the positioning of PD between Japan and overseas.[6]

Standard for Microbiological Management of Fluids for Hemodialysis

There has been wide concern that contaminants in dialysis fluids may enter the body and cause complications or adverse effects by various mechanisms in dialysis patients. The risk of contaminants entering the body increases with the improvement in the solute removal performance of the dialyzer. The JSDT published a guideline in 2008, which provided standards on and procedures of microbiological management of dialysis fluids, to perform safe and effective hemodialysis.[7] The standards mentioned in the guideline require the following attainment levels.

- Dialysis water (Reverse Osmosis [RO] Water): Bacteria <100 CFU/mL, Endotoxin <0.050 EU/mL
- Standard dialysis fluid: Bacteria <100 CFU/mL, Endotoxin <0.050 EU/mL
- Ultrapure dialysis fluid: Bacteria < 0.1 CFU/mL, Endotoxin <0.001 EU/mL (less than the detection limit).

In addition, online prepared substitution fluid should be sterile and non-pyogenic, with attainment levels of $<10^{-6}$ CFU/mL for bacteria and <0.001 EU/mL (less than the detection limit) for endotoxin. In Japan, the expense of the management of dialysis fluids has come to be covered by health insurance since April 2010, on the condition that the standards specified in the guideline should be attained and an appropriate manual for the management of dialysis fluids should be kept.

In conclusion, the current status of and problems with dialysis therapy in Japan, and the guidelines proposed by the JSDT to solve the problems have been mentioned above. The JSDT is now preparing a guideline for cardiovascular disease management, a guideline for the criteria for starting dialysis and the appropriate prescription of hemodialysis, a guideline for blood glucose control in diabetic patients on dialysis, etc. These new guidelines, as well as the updated versions of the existing guidelines, will soon be published on the website at http://www.jsdt.or.jp/guideline.html. The JSDT would appreciate questions and comments on the guidelines and hope that these guidelines will be utilized not only in Japan but also overseas.

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