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COMMENT

Brain atrophy in patients on peritoneal dialysis treatment

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Cognitive impairment affects patients' skills in understanding health literacy, making decisions about their healthcare, and adhering to complex medical regimens, such as dietary and fluid regulations [1]. Patients with cognitive impairment are also at an increased risk of hospitalization and/or mortality. In this regard, it has become a serious concern among patients with end-stage kidney disease (ESKD), who need to access health services more frequently than almost any other population [2]. A high prevalence of such a disease state has been shown in patients with ESKD, and studies in patients receiving chronic hemodialysis (HD) treatment have demonstrated that the frequency of moderate-to-severe cognitive impairment is as high as 70%, potentially reaching several times higher than in age-matched controls [2].

Although the relationship between chronic kidney disease (CKD) and a decline in cognitive functioning has been widely accepted, it has also been suggested that HD itself may also accelerate cognitive decline [3]. Several factors related to cognitive impairment have been proposed, and brain atrophy has been shown to be associated with cognitive impairment in various disease conditions, including ESKD [4]. Interestingly, it has been demonstrated that the progression of brain atrophy is rapid in patients with CKD, especially in those undergoing regular HD treatment [4]. In addition, a higher incidence of brain atrophy in such patients, even at a younger age, than in the general population, as well as a significant relationship between frontal lobe atrophy and the frequency of rapid decline in blood pressure during the HD session has been demonstrated [5, 6]. On the other hand, it has been shown that the incidence of brain atrophy is higher in patients with peritoneal dialysis (PD) dependent CKD than in those with non-dialysis dependent CKD. Furthermore, a longitudinal examination comparing annual changes in brain volume over two years between these two groups revealed that the magnitude of brain atrophic change was two to three times greater in the former than in the latter [7]. However, whether or not there is any difference in the severity of brain atrophy between patients undergoing HD and those undergoing PD remains to be determined.

Tsuruya et al. focused on this concern in their study, "Faster brain atrophy in patients on peritoneal dialysis compared with hemodialysis: The VCOHP Study," published in the current issue of *Hypertension Research* [8]. In this study, they examined not only the brain volume, which was standardized by determining the percentages of gray matter to total intracranial volume, but also its annual change in patients on PD, and compared the findings with those in patients on HD in both cross-sectional and longitudinal analyses. A cross-sectional study showed that age- and sex-adjusted brain volumes were significantly lower in PD patients than in HD patients. In addition, they demonstrated that the regression slope between age and brain volume was steeper in PD patients than in HD patients. In contrast, a longitudinal analysis revealed that age- and sex-adjusted brain volumes at baseline and after two years were significantly lower in PD patients than in HD patients. They also showed that the annual decrease in brain volume was significantly greater in PD patients than in HD patients, even after adjusting for potential confounding factors, including age, sex, diabetes mellitus, a history of cardiovascular disease, smoking habits, systolic blood pressure, hemoglobin concentration, baseline brain volume, and log-transformed brain natriuretic peptide [8]. This study is interesting in terms of the fact that it is the first detailed report comparing brain atrophy between PD and HD patients, while the findings may be somewhat surprising given the therapeutic nature of PD.

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PD is an accepted modality for managing ESKD, in which various solutes diffuse from the blood which abundantly flows through the capillary plexus in the peritoneum into the dialysate fluid instilled in the patient's abdomen, thereby working analogous to that of the extracorporeal method [9]. It offers a rational therapeutic approach in the broader context of overall health care, including minimal intravascular volume status variation, cardiovascular stress reduction, avoidance of peaks and troughs of uremic toxins, prevention of arrhythmia, improved preservation of the residual kidney function, and freedom from perpetual hospital visiting [9, 10].

HD is a dialysis method that removes waste products from a patient's blood through a dialyzer unit packed with hollow polymeric fibers. This procedure must typically be performed in dialysis clinics and/or regional hospitals [11]. Intradialytic hypotension, which is defined as either a drop in systolic blood pressure of ≥20 mmHg or in mean arterial blood pressure of ≥10 mmHg in combination with clinical manifestations of hypotension, is a well-known complication of HD with an incidence of approximately 10% among patients with ESKD receiving periodic outpatient programs [11]. Despite technological advances in dialysis practices that allow us to perform real-time estimation of the effective circulating volume and adjustment of dialysate composition to manage vascular tonicity, it remains the most common adverse event associated with HD sessions. As a matter of course, it is associated with not only transient ischemic stress to vital organs, such as the heart and brain, but also elevated patient mortality [11].

Both PD and HD are dialysis options for patients with ESKD for whom other renal replacement therapies, including kidney transplantation, are not available, although PD is not often used in developed countries, as extracorporeal methods are preferentially adopted [9]. Nevertheless, evidence to support a general recommendation of one dialysis procedure over another for medical reasons is lacking, and the choice of PD or HD may depend on various factors, including the patient's physical condition, social circumstances, motivation, or desire and physician and/or nurse bias [12]. The differences between the PD and HD groups are shown in Fig. 1.

Before arriving at the conclusion of the current study that the decline in brain volume was faster in PD patients than in HD patients [8], Tsuruya et al. might have hypothesized that it could be prevented in PD patients, but not HD patients, since it has been considered that brain hypoperfusion during HD sessions likely plays a role in brain atrophy in HD patients [5, 6]. Indeed, a significant relationship has previously been reported between the number of dialysis-related hypotension episodes and changes in frontal brain volume, suggesting that dialysis-related hypotension may play a role in the progression of frontal lobe atrophy in HD patients [5, 6]. Furthermore, there is a significant relationship between brain atrophy and the cognitive function in patients with non-dialysis-dependent CKD [4]. Considering that patients on PD are generally hemodynamically stable [9, 10], the findings of the current study may be rather surprising and prompt us to speculate that there may be some factor associated with brain atrophy in patients with

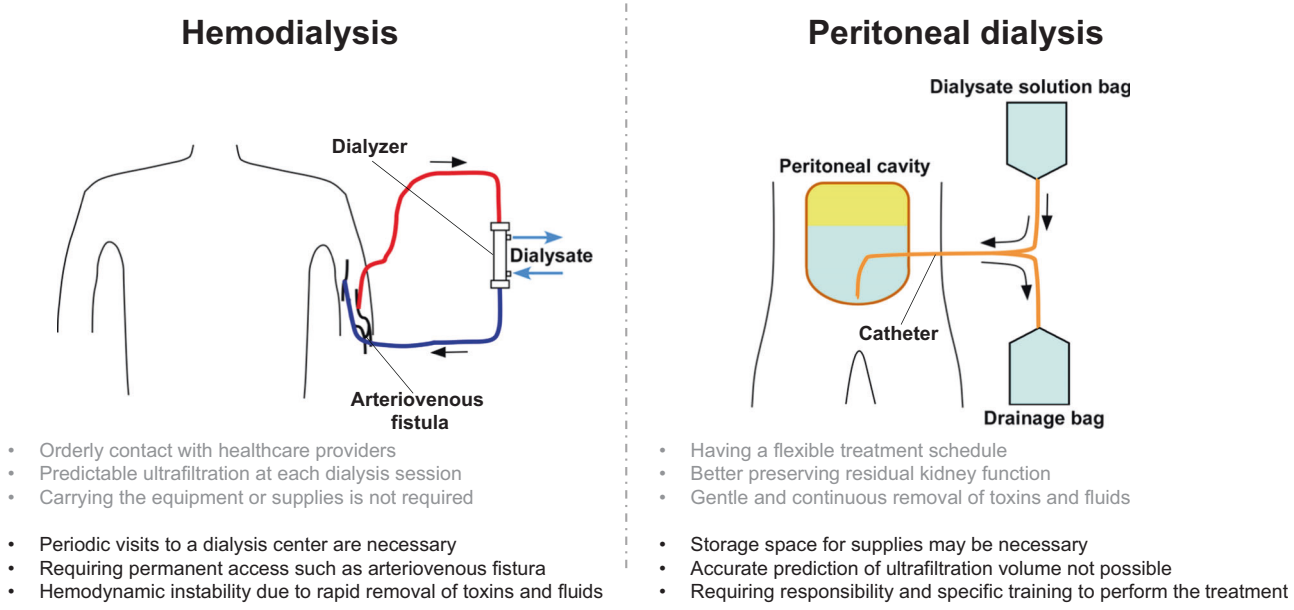

Fig. 1 Difference between HD and PD. HD is a procedure in which equipment and a dialyzer are used to purify a patient's blood. Typically, an arteriovenous fistula and/or a synthetic graft is used to gain access to the blood for treatment. In PD, the peritoneum in the patient's abdomen is used as the membrane through which excess fluid and solutes are removed from the blood. Some advantages (gray) and disadvantages (black) of each method are listed below in the corresponding schematic representations

ESKD other than a decline in brain perfusion due to dialysis-related hypotension.

Determining the precise relationship between brain atrophy and the cognitive function, especially in patients on PD, is another prerequisite, since several reports have shown that the cognitive function is more preserved in PD patients than in HD patients [1–3]. In contrast, no significant difference in dementia risk between HD patients and PD patients was demonstrated in a nationwide population-based study in Taiwan [13]. The reasons for this inconsistency remain to be delineated; however, such findings may be compromised by small sample sizes, selection bias, and observational nonrandomized designs [13]. Alternatively, or in addition, we may need to pursue qualitative and quantitative assessments for morphological changes of the brain more carefully, since brain atrophy is not a homogenous process, and such a change may be modified by the uremic milieu [14]. Furthermore, as the authors pointed out, we may otherwise be required to conduct investigations with the view that brain atrophy represents a final common pathway for the pathological processes resulting from various brain diseases, including small-vessel diseases that have not yet been evaluated thoroughly [8, 15].

We believe that the results of the present study by Tsuruya et al. do not discourage us from adopting PD as a dialysis option in an ordinary clinical setting. Randomized controlled trials may be ideal to disclose the clinical benefits of PD more precisely; however, there is no way to justify the random selection of dialysis modalities. Rather, we should perform prospective observational studies with a larger number of subjects more extensively, thereby allowing us to better understand not only the clinical significance of PD in the overall management strategy for ESKD but also its impact on brain atrophy and cognitive disturbances.

Compliance with ethical standards

Conflict of interest The author declares no competing interests.

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