Netherlands
The Journal of Medicine

REVIEW

The possible impact of dialysis modality on cognitive function in chronic dialysis patients

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ABSTRACT

Chronic kidney disease (CKD) is a growing public health problem. Individuals in all stages of CKD are at higher risk for development of cognitive impairment and this may be a major determinant in their quality of life (QOL). The prevalence of cognitive deficits is particularly high in subjects with end-stage renal disease (ESRD). While it is sufficiently well documented that ESRD is linked with a change in cognitive function, little is known about the influence of different dialysis modalities on cognitive function. The effect of dialysis modality on risk of cognitive impairment is unclear. Some data suggest that patients with ESRD treated with chronic ambulatory peritoneal dialysis (CAPD) had consistently better cognitive function than patients treated with haemodialysis (HD). We concluded that the previously observed apparent difference between two modalities of dialysis treatments resulted either from very low dialysis delivery or comparison with poorly matched controls. Regarding these data from previous studies we hypothesised that well-dialysed, well-nourished and medically stable HD patients had no cognitive dysfunction in comparison with well-dialysed, well-nourished, medically stable and demographically matched CAPD patients. Also, future studies are needed to differentiate between modality as a risk factor from the factors contributing to selection bias among patients choosing CAPD over HD.

KEYWORDS

Chronic kidney disease, cognitive function, dialysis modality

Chronic kidney disease (CKD) is the permanent loss of kidney function and it is a rapidly growing global health problem, with a prevalence of 15% in developed nations.[1,2] The final stage of chronic kidney disease is end-stage renal disease (ESRD). ESRD is a progressive, debilitating, chronic illness that requires nursing and medical interventions that include dialysis, education on lifestyle alterations, and dietary and fluid restrictions.

In ESRD, kidney function can be replaced by three main medical treatment modalities: haemodialysis (HD), chronic ambulatory peritoneal dialysis (CAPD) or by kidney transplantation. The best treatment for a patient who is very close to ESRD is pre-emptive transplantation, but transplantation generally does not happen because of an insufficient number of donors. The two major dialysis types, HD and PD, are not only different from one another technically, but also with regard to the expectations of patients pertaining to the effort involved. Each dialysis type has its advantages and disadvantages and has a different level of impact on patients' physical, psychological and social health, and each places its own limitations on lifestyle.[3]

Results from single centre and multicentre studies with CAPD and HD patients show conflicting results with respect to the survival benefits of one form of therapy over the other.[4-9] Based on review of recent publications and additional analyses of US Medicare data, patient survival is similar for CAPD and HD but important differences do exist within select subgroups of patients, particularly those subgroups defined by age and the presence or absence of diabetes.[8]

ESRD can have an impact on patients' quality of life (QOL), potentially affecting their physical and mental health, functional status, independence, general well-being, personal relationships and social functioning. Awareness of patient satisfaction and QOL has been increasing and health-related QOL issues are now recognised as important outcome measures in health care, cost-effective analyses of the efficacy of medical care and clinical trials,

and therapeutic interventions for chronic conditions, including end-stage renal disease (ESRD). QOL is also a factor in the decision-making process for dialysis treatment selection.[11] Defining QOL is complex as it can encompass a wide range of factors including psychological, cognitive, social, economic, political, cultural, spiritual, and physical factors.[12]

Comparative studies suggest that health-related QOL differs within dialysis patients, such as CAPD *vs* HD. However, evidence to suggest one mode of dialysis modality is better than the other in impacting on/improving health-related QOL is still inconclusive.[13] Lately, awareness of patient satisfaction and QOL has been increasing. Some recent studies have evaluated patients' treatment satisfaction level. In most of these studies, CAPD patients seem to be much happier than HD patients are.[14-16] These results do not change after adjustment for age, ethnicity, education level, marital status, employment status, distance from the treatment centre, and treatment duration.[15] Patients in the HD treatment modality, particularly those with many years of treatment, experienced a more compromised QOL in comparison with CAPD patients.[17] In a meta-analysis of 61 studies, CAPD patients were characterised by a better well-being and less distress than HD patients.[18] Some studies suggested that both HD and CAPD patients had similar health-related QOL.[19,20] Regarding psychological dimensions in ESRD, it seems that CAPD patients are better adjusted than HD patients. This may be because the peritoneal treatment modality offers increased autonomy and control, flexibility in everyday life and the dietary regime, as well as fewer social restrictions.[18,21-23] CAPD patients have been found to report better QOL ratings in specific areas such as 'perceived ability to travel', 'financial concerns', 'restriction in eating and drinking' and 'dialysis access problems'.[24] Furthermore, PD patients have indicated more positive ratings in several disease QOL domains, e.g. less kidney disease burden, and being more encouraged and satisfied with care.[25] Compared with HD patients, CAPD patients experienced more personal control and had a better understanding of the illness.[26] The only randomised trial investigating health-related QOL of CAPD and HD patients found a small difference favouring HD patients after two years follow-up.[27]

Change in cognitive function is one of the well-known consequences of ESRD[28,29] and this may be a major determinant in patients' QOL. Cognitive impairment is defined as a new deficit in at least two areas of cognitive functioning. These may include disturbances in memory, executive functioning, attention or speed of information processing, perceptual motor abilities or language.[30] It has been shown that cognitive impairment is associated with the severity of kidney disease[31,32] and that prevalence of cognitive deficits is particularly high in subjects with ESRD.[33] Cognitive impairment is likely to become an increasingly important public health issue in dialysis patients as the ESRD population ages, and the prevalence of diabetes and vascular disease increases in incident dialysis patients.[30] The accumulation of toxic substances resulting from significantly reduced metabolic rates, as well as chronic dialysis, has been shown to impair functions of the central nervous system in this population. The patients with CKD have been demonstrated to develop uraemic or dialysis-related encephalopathy accompanied by frontal and basal ganglia abnormalities on neuroimaging.[34-37] The impairment of cognitive functioning is also attributed to the effect of uraemic toxins on neurons. However, the persistence of cognitive impairment despite clinically adequate dialysis dose delivery indicates that other factors also contribute to the brain dysfunction.[38] Cerebrovascular disease is a powerful risk factor for the development of cognitive impairment[39,40] in the general population and as eluded to above vascular disease is a more likely cause of cognitive impairment than Alzheimer's disease in patients with CKD. Traditional vascular risk factors linked to development of cerebrovascular disease include hypertension,[41] diabetes, hypercholesterolaemia,[42] cardiovascular disease and cigarette smoking.[43] Other nontraditional vascular risk factors that may be associated with cognitive impairment include hyperhomocysteinaemia, haemostatic abnormalities, hypercoaguable states, inflammation, and oxidative stress.[44-46] A more recent focus relates to the potential roles of secondary hyperparathyroidism as risk factor for cognitive impairment in the CKD population. Animal studies have identified parathyroid hormone as neurotoxic, and the increased brain calcium content, driven by elevated parathyroid hormone levels, in patients with CKD has been postulated to interfere with neurotransmission in the central nervous system.[47,48] Anaemia in patients with ESRD has been associated with cognitive impairment and neuropsychological and neurophysiological tests have shown improvement with the treatment of anaemia with CKD.[38,49,50] It is well known that as patients progress through the stages of CKD nutritional requirements are altered and the metabolism of protein is affected.[51] Serum albumin is the most extensively studied nutritional marker in these patients due to its easy viability and strong association with hospitalisation and risk of death.[52] According to these studies serum albumin is strongly associated with cognitive performance in patients with ESRD. In a study with HD patients,[53] Mini Mental State Examination score was associated with serum albumin, protein catabolic rate and interdialytic weight gain. Pliskin *et al.* observed no clear neuropsychological deficit in well-nourished, well-dialysed and medically stable HD

patients when compared with age- and education-matched medical controls with no ESRD.[54] In a study performed by Umans *et al*. attention and mental processing speed were also not different in ten stable HD patients compared with age- and education-matched controls.[55] Also hypervolaemia may be one of the causal and potentially modifiable factors of cognitive dysfunction. Strict volume control may have beneficial effects on cognitive functions in HD patients.[56] Earlier studies have shown that cognitive impairment is a complication of advanced pre-ESRD and ESRD patients on maintenance dialysis.[29-31,50,57-59] Cognitive function is reduced even in patients with only moderate reduction in glomerular filtration rate. Thus awareness and treatment of cognitive deficit should begin early in the progression of kidney disease.[60]

The diagnosis of cognitive impairment is important because this is associated with an increased risk of death in dialysis patients and with a decreased QOL in this population.[61,62] Furthermore, cognitive impairment may impact decision-making as well as the ability to adhere to dialysis recommendations, such as dietary modification and medication compliance. Cognitive impairment is also associated with increased staff time in caring for the patients, greater utilisation of healthcare resources, more frequent hospitalisations and an increased number of days spent in the hospital.[63]

Cognitive impairment is often not detected by clinicians and cognitive assessment should be included in the routine evaluation of elderly patients with renal failure, with potential implications for the treatment and quality of treatment for these patients.[64]

While it is sufficiently well documented that ESRD has been linked with change in cognitive function, little is known about influence of different dialysis modalities on cognitive function. Although a considerable number of articles on ERSD have been published, there are a limited number of studies comparing cognitive function in HD and CAPD patients. Some data suggest that the prevalence of cognitive impairment may be different in patients treated with HD compared with patients treated with CAPD.[65-67] They also demonstrated that CAPD patients had consistently better cognitive function than HD patients. The results from these studies may not reflect the dialysis procedure itself but selection bias as to who is receiving which modality of dialysis treatment. A selected group of patients was not matched for important demographic variables, including age or level of education. The differences in cognitive functions between the two dialysis modalities could also be due to differences in cognitive functions prior to the start of dialysis, which makes a comparison between the modalities difficult. Also, patients with medical comorbidities such as unstable coronary or cerebrovascular disease, neurological deficits, refractory anaemia, malnutrition, autoimmune diseases, malignancies, liver disease or other metabolic disease leading to encephalopathy were not excluded from these studies.

CONCLUSION

We presumed that the previously observed apparent difference in cognitive functions between the two modalities of dialysis treatment resulted either from very low dialysis delivery or comparison with poorly matched controls. Regarding these data drawn from the literature, we hypothesised that well-dialysed, well-nourished and medically stable HD patients had no cognitive dysfunction in comparison with well-dialysed, well-nourished, medically stable and demographically matched CAPD patients. Future investigations on cognitive function in uraemic patients treated with HD and CAPD are needed, with a larger number of participants in a prospective research model. Those studies are needed to differentiate between modality as a risk factor from the factors contributing to selection bias among patients choosing peritoneal dialysis over haemodialysis. Increased awareness of cognitive impairment effects on daily function, quality of life, medication, fluid and dietary compliance is needed.

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